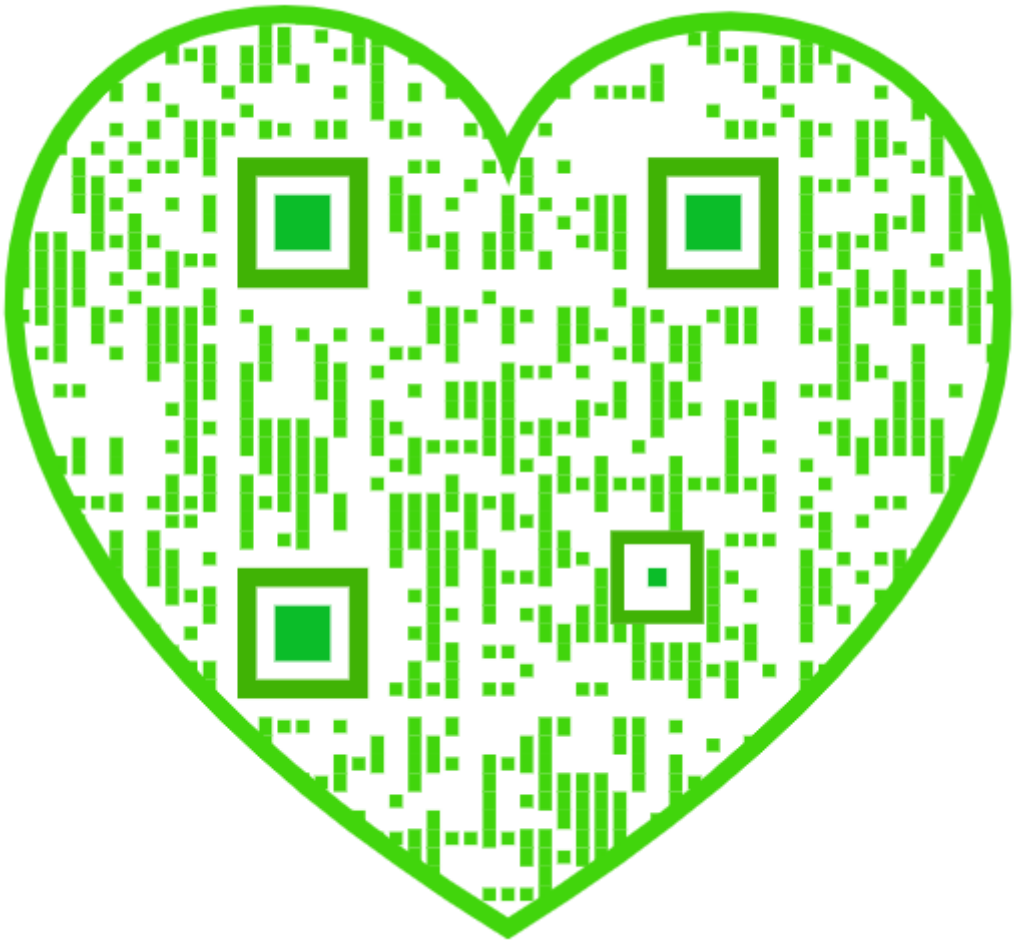
The AMERICAN YEAR-BOOK of ANESTHESIA & ANALGESIA

F. H. McMECHAN, A.M., M.D.
EDITOR



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i

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INDEX TO ADVERTISEMENTS

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MANUFACTURERS

	Page
Abbott Laboratories	6
Fairchild Bros. & Foster	5
Foregger Company, Inc	13
Heidbrink Company	15
Hoffman-La Roche Chemical Works	5
Horlick's Malted Milk Company	19
A. Klipstein & Company	3
Knoll & Company	19
Charles B. Knox Company, Inc	8
Kny-Scheerer Corporation	14
Life Saving Devices, Inc	10
McDermott Surgical Instrument Co., Ltd	19
Mallinckrodt Chemical Works	20
Meinecke & Company	18
Mulford-H. K. & Co	17 B
Parke, Davis & Company	4
E. R. Squibb & Sons	1–2–9
Standard Oil Company	7
Stratford-Cookson Company	19
Surgery Publishing Company	16–17
Taylor Instrument Companies	18
Teter Manufacturing Company	15
Toledo Technical Appliance Co	12
S. S. White Dental Mfg. Co	11

MEDICINAL PRODUCTS

	Page
Adrenalin	4
Bacterins	17 B
Barium Sulphate	20
Bromural	19
Chloroform, Squibb	2
Coagulen Ciba	3
Coagulose	4
Digifoline Ciba	3
Ether for Anesthesia	2–4–20
Ethyl Bromide, Squibb	2
Ethyl Chloride, Squibb	2
Gelatine	8
H-M-C	6
Liquid Petrolatum, Squibb	1–9
Malted Milk (Horlick's)	19
Mineral Oils	1–7–9
Nujol	7
Olive Oil, Squibb	2
Panopepton	5
Pituitrin	4
Purified Pyroxylin	20
Scopolamine Stable "Roche"	5
Serums	17 B
Somnoform	19
Vaccines	17 B

APPARATUS

Anesthetic Autogenor	13
Automatic Anesthetizer	15
Bed and Douche Pan	18
Ether Apparatus	19
Gas-Oxygen Apparatus	13–15
Life Saving Autogenor	13
Lungmotor	10
Nitrous-Oxid-Oxygen Apparatus	11–12
Publishers	16–17
Resusctation Apparatus	10–13–14
Sphygmomanometer	18
Vapor Anesthesia Apparatus	14

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6. **Gynecology** — (a) perineorrhaphy; (b) removal of inguinal glands; (c) removal of clitoris.
7. **Rectum** — (a) hemorrhoids; (b) fistula in ano.
8. **Genitourinary** — (a) circumcision; (b) bubo; (c) hydrocele; (d) varicocele; (e) urethral stricture; (f) hypospadias and epispadias.
9. **Extremities** — (a) ingrowing toe nail; (b) hammer toe; (c) amputations.
10. **Eye, Ear, Nose and Throat** — (a) chalazion; (b) cataract; (c) iridectomy; (d) mastoiditis; (e) tonsillectomy; (f) nasal polypi; (h) neoplasms of vocal cords.
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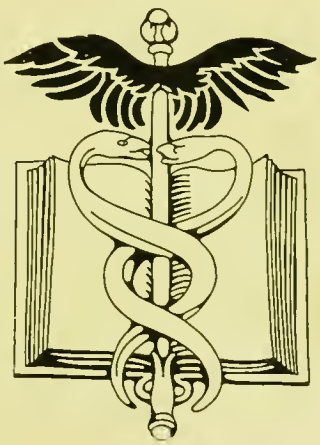
The AMERICAN YEAR-BOOK of ANESTHESIA & ANALGESIA

F. H. McMechan, A.M., M.D.
Editor

1915 1915



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The AMERICAN YEAR-BOOK of ANESTHESIA & ANALGESIA

EDITORIAL FOREWORD

WHILE The Quarterly Supplement of Anesthesia and Analgesia of the AMERICAN JOURNAL OF SURGERY has provided a journalistic medium for the publication of the *Transactions* of various associations of anesthetists, it does not lend itself to the collation of the world's ultra-scientific researches in these subjects.

Consequently The American Year-Book of Anesthesia and Analgesia has been established for this very purpose, and eminent surgeons, dentists, anesthetists and research-workers have collaborated in presenting, herewith, the current advances in the science of practice of anesthesia and analgesia.

It had been expected to have the list of contributors more international in character, but the unfortunate war conditions on the Continent prevented. However, those authorities who have contributed, have scoured the world's literature to make the context of the Year-Book as comprehensive and exhaustive as possible.

Original researches have been given especial prominence in the hope that their publication, more or less in detail, will be an incentive to renewed efforts on the part of those who are seeking to replace the controversial phases of anesthesia and analgesia with indisputable facts.

Nor have the clinical aspects of these subjects been neglected. On the contrary the master-technicians have contributed their quota of invaluable information regarding those methods that have withstood the crucial test of *service*.

The Year-Book has been so edited as to appeal to all those progressive members of the allied professions and specialties, who in any manner come in contact with the science or practice of anesthesia and analgesia. Besides a general survey of the progress in these subjects, the Year-Book provides the surgeon, dentist, anesthetist and research-worker with those special advances that have a direct bearing on his individual requirements.

Volume One of the Year-Book has been compiled exclusively of exhaustive articles by prominent authorities in an effort not only to record current advances, but also to bring a given number of subjects in anesthesia and analgesia strictly up-to-date. In succeeding volumes of the Year-Book, Collective Abstracts will continue the revision of these subjects as necessity arises and other subjects of equal importance and interest will be introduced and as compre-

hensively and exhaustively handled. The Year-Book will thus assume the form of a continuously broadened and revised encyclopedia for authoritative reference. In order to make it subserve this purpose the Editor hopes that its subscribers will send him their personal suggestions for rendering each succeeding volume more *serviceable*.

The innovation of the Advertising Sections has been made advisedly. Efforts for advancing the science and practice of anesthesia and analgesia have no endowment fund to back them, and the Year-Book, to assure its permanence and in order to fulfill its expectations, has considered it essential to establish itself, first and foremost on a secure financial basis. Whatever success the Year-Book now achieves will enable the Publishers and Editor to make succeeding volumes all the more valuable to the subscribers. The pertinent products in the Advertising Sections of the Year-Book all conform to the standards of the Council of the American Medical Association, and on account of the cordial cooperation of these advertisers in making the publication of the Year-Book a possibility and assuring its continuance, the Editor and Publishers bespeak for them the good will and interested attention of all subscribers.

Personally the Editor wishes to thank all those, who, in any way, have contributed to the context of the Year-Book. Its editing has been a labor of love, and has proven itself the best of tonics during a prolonged convalesence from a protracted illness. In conclusion the Editor solicits the continued support of all those who appreciate the *service* which the Year-Book provides.

Curtis Farms,
Avon Lake, Ohio,
July, 1916.

F. H. McMECHAN, M. D.
Editor.

1915 ▩ ▩ TABLE OF CONTENTS FOR VOLUME ONE ▩ ▩ 1915

Pages

THE PHYSICO-CHEMICAL THEORY OF ANESTHESIA 1–30
Ralph S. Lillie, Ph. D., Worcester, Massachusetts.

BLOOD CHANGES UNDER ANESTHESIA AND ANALGESIA 31–53
Theodore D. Casto, D. D. S., Philadelphia, Pa.

THE PERIPHERAL ORIGIN OF SHOCK 54–69
Frank C. Mann, M. D., Rochester, Minnesota.

CIRCULATORY DISTURBANCES DUE TO OPERATIVE PROCEDURES, POSTURE AND DEPTH OF ANESTHESIA 69–76
Willis Drew Gatch, M. D., Indianapolis, Indiana.

ANESTHESIA, ANEMIA AND RESUSCITATION 77–86
George W. Crile, M. D., Cleveland, Ohio.

BLOOD PRESSURE UNDER ANESTHESIA FROM RECORDS OF 6,000 PERSONAL OBSERVATIONS 87–94
E. I. McKesson, M. D., Toledo, Ohio.

SOME CONSIDERATION OF RESPIRATION IN RELATION TO APNEA, ANOXHEMIA, ACAPNIA AND ANESTHESIA 95–106
Yandell Henderson, Ph. D., New Haven, Connecticut.

MORTALITY UNDER ANESTHETICS 107–115
Albert H. Miller, M. D., Providence, Rhode Island.

CARDIAC FIBRILLATION AND CHLOROFORM SYNCOPE 116–135
A. Goodman Levy, M. D., London, England.

DELAYED CHLOROFORM POISONING 136–151
Evarts A. Graham, M. D., Mason City, Iowa.

SOME PSYCHIC FACTORS OF SURGICAL ANESTHESIA 152–160
Robt. H. Ferguson, M. D., D. Sc., East Orange, N. J.

THE USE OF MUSIC DURING ANESTHESIA AND ANALGESIA 164–167
W. P. Burdick, M. D., Kane, Pennsylvania.

FROM THE OUTSIDE LOOKING IN 168–170
Jesse A. Jarvis, Portland, Oregon.

KIDNEY FUNCTION AND ANESTHESIA 171–175
James J. Hogan, M. D., M. R. C. S., San Francisco, Cal.

MANUFACTURE OF NITROUS OXID FOR HOSPITAL USE 176–181
A. R. Warner, M. D., Cleveland, Ohio.

Pages

ETHER-OIL COLONIC ANESTHESIA 182–212
James Tayloe Gwathmey, M. D., New York City.

PERFECTED METHODS OF ETHERIZATION 213–226
Ray A. Rice, M. D., Columbus, Ohio.

NITROUS OXID IN OBSTETRICS 227–245
Arthur E. Guedel, M. D., Indianapolis, Indiana.

ALKALOIDAL AMNESIA IN OBSTETRICS 246–250
John Osborn Polak, M. D., and Harvey B. Matthews, M. D., Brooklyn, N. Y.

THE NASAL ADMINISTRATION OF NITROUS OXID-OXYGEN 251–273
F. H. McMechan, M. D., Avon Lake, Ohio.

THE OBSTREPEROUS DENTAL PATIENT 274–282
Edward S. Barber, D. D. S., Chicago, Illinois.

THE NASAL ADMINISTRATION OF SOMNOFORM FOR DENTAL OPERATIONS 283–296
Wm. Harper DeFord, D. D. S., M. D., Des Moines, Iowa.

FURTHER RESEARCHES IN NOVOCAIN-SUPRARENIN ANESTHESIA 297–318
Richard H. Riethmüller, D. D. S., Philadelphia, Pa.

INTRA- AND EXTRA-ORAL METHODS OF LOCAL ANESTHESIA FOR DENTISTRY; WITH SPECIAL REFERENCE TO APIECTOMY 319–337
Kurt H. Thoma, D. M. D., Boston, Massachusetts.

LOCAL ANESTHESIA AND AFTER-PAIN 338–348
Arthur E. Hertzler, M. D., Kansas City, Missouri.

LOCAL ANESTHESIA FOR ANO-RECTAL SURGERY 349–363
Louis J. Hirschman, M. D., Detroit, Michigan.

LOCAL ANESTHESIA IN THE RADICAL SURGERY OF HERNIA 364–379
Charles T. Souther, M. D., Cincinnati, Ohio.

LOCAL ANESTHESIA FOR PROSTATECTOMY 380–389
Carroll W. Allen, M. D., New Orleans, Louisiana.

INJECTING THE GASSERIAN GANGLION FOR TRIFACIAL NEURALGIA 390–398
Wilfred Harris, M. D., London, England.

SPINAL ANESTHESIA IN THE CAT 399–409
W. T. Porter, Ph. D., New Haven, Connecticut, and
George G. Smith, M. D., Boston, Massachusetts.

SPINAL ANESTHESIA IN UROLOGY 410–415
George G. Smith, M. D., Boston, Massachusetts.

HE MEN WHO HAVE ACHIEVED SUCCESS ARE THOSE WHO HAVE WORKED, READ AND THOUGHT MORE THAN WAS ABSOLUTELY NECESSARY, WHO HAVE NOT BEEN CONTENT WITH KNOWLEDGE SUFFICIENT FOR THE PRESENT NEED, BUT HAVE SOUGHT ADDITIONAL KNOWLEDGE AND STORED IT AWAY FOR THE EMERGENCY RESERVE. IT IS SUPERFLUOUS LABOR THAT EQUIPS A MAN FOR EVERYTHING THAT COUNTS MOST IN LIFE.—*Davis.*

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THE THEORY OF ANESTHESIA • PREVALENCE OF REVERSIBLE INHIBITION OF SUSPENDED ACTIVITY • EXTERNAL CONDITIONS EFFECTING CELL CHANGES • ANESTHETIC EFFECTS OF NEUTRAL SALTS AND LIPOID SOLVENTS • VARIOUS HYPOTHESES • AGGREGATION OF COLLOIDS • PHENOMENA OF ASPHYXIA AND DEOXIDATION • MATTHEWS' THEORY • DEGREE OF ORGANIZATION AND SUSCEPTIBILITY TO NARCOSIS • THE PHYSICO-CHEMICAL ALTERATION OF PLASMA-MEMBRANE AS A BASIS OF ANESTHESIA • REDUCED ELECTRICAL CONDUCTIVITY AND DECREASED PLASMA-MEMBRANE PERMEABILITY • THE MECHANISM OF THE PHYSICO-CHEMICAL BASIS OF ANESTHESIA • BIBLIOGRAPHIC REVIEW.

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ANESTHESIA OR NARCOSIS is a condition in which the normal responsiveness or automatic activity of the living system—*organism, tissue, or cell*—is temporarily decreased or abolished. The subjective accompaniment of this change in higher animals is a more or less complete suppression of consciousness, with consequent insensibility to pain; the term anesthesia refers more directly to this condition. By *narcosis* is usually meant a temporary paralysis or anesthesia produced by chemical substances; this term has a more objective connotation, and is the one usually employed in purely physiological discussions. It is especially noteworthy that the condition may show all gradations of degree, ranging from a comparatively slight inhibition or insensibility to a state of profound depression in which the organism is completely inert and shows no response to even the strongest stimuli. Yet on the removal of the anesthetizing agent the normal properties and activities return. *Reversibility* is thus an essential characteristic of the condition; this peculiarity distinguishes it from the irreversible change of death. There are, however, significant resemblances between these two states, and in fact transitions from the one to the other are frequent. Too prolonged or too profound anesthesia may pass into death; and most anesthetic substances, if present in too high concentration, soon cause irreversible and cytolytic changes in cells. There is in fact evidence that in many instances anesthetic and toxic effects have the same essential physico-chemical basis. The same cell-structures—especially surface-structures, (plasma-membranes)—are primarily affected in both cases, but in the one the change produced is reversible, in the other irreversible. The degree of reversibility, however, is itself subject to variation. In many colloidal systems changes which are reversible in their earlier stages may become irreversible later; and the fact that anesthesia, especially if profound, cannot be prolonged indefinitely without danger to life, may find its explanation here.

THE PREVALENCE OF REVERSIBLE INHIBITION OR SUSPENDED ACTIVITY.

In any theoretical discussion of anesthesia it is important to recognize from the first that normal or physiological conditions of reversible inhibition or suspended activity are in no sense unusual among organisms. In both animals and plants irritability and automatic activity are fluctuating properties., showing a wide range of strictly physiological variation.

Thus in higher animals we have conditions ranging from the profound narcosis of sleep —a state due apparently to the accumulation of fatigue-products in the blood—to one of complete mental and physical alertness or wide-awakeness. Responsiveness is largely a matter of metabolic condition; and most vital activities are subject to inhibition or enhancement according to physiological requirements. Variability of this kind is in fact a necessary condition of adaptation to the changing conditions of life. Thus the activities of animals as a class are especially influenced by variations in the food-requirements. In general they become sluggish and irresponsive when well fed, and show heightened activity when deprived of food. In other words, both the automatic motor activity and the responsiveness to the stimuli of food-substances—the physiological condition expressed in consciousness as *hunger*—are increased when the supply of energy-yielding material is depleted, and *vice versa*. For example, the fresh water Hydra, one of the most primitive metazoa, shows restless swaying movements when hungry; these movements increase the area swept by the tentacles, and these organs respond promptly to the contact of small organisms or food-particles by capturing and conveying to the mouth.[1] When well fed the creature is quiescent, and the tentacles are indifferent to such contact; they are, as it were, in an anesthetized condition; this state passes off as the organic demand for food reasserts itself. Such an instance illustrates the regulatory rôle which fluctuations in the responsiveness of an animal to stimuli play in its normal life. Similar variations in neuromuscular responsiveness occur throughout the animal kingdom. This is well illustrated by the case of sleep, which is in fact a physiological narcosis, characterized by a definite periodicity and by affecting especially certain parts of the central nervous system; the use of opiates illustrates how readily a chemically induced narcosis may pass into the physiological form. From such facts we must conclude that the essential basis of anesthesia is to be sought not in purely artificial modifications of nervous irritability, but in some normal or physiological modification which is capable of being intensified and prolonged by the use of certain physical and chemical agencies; these are the various anesthetizing agencies, such as the electric current, cold, or narcotizing substances. From this point of view, anesthesia is to be regarded not as an essentially abnormal or artificial phenomenon, but simply as an intensification of a normal physiological condition; and its essential basis sought in the normal inhibitions and depressions shown by all living cells.

Instances of such normal inhibitions are innumerable. The motor neurones innervating any group of muscles become inexcitable during the activity of the antagonist groups, as Sherrington has shown; the respiratory nerve-cells cease automatic activity with over-oxygenation of the blood; vaso-motor, cardiac, glandular, and muscular activities are subject to various forms of inhibition, partly nervous and partly chemical in origin. Such inhibitory mechanisms play in normal life a part whose importance is daily more widely recognized by physiologists. Mechanisms of the inverse kind, which exercise sensitizing and reinforcing influence on various functions, are also frequent in organisms. A large part of these normal inhibitions and excitations are now known to be due to chemical substances (hormones) present in the blood and derived from ductless glands or other sources of internal secretion. The regulation and integration of bodily activities are thus largely under direct chemical as well as nervous control. Such normal chemical inhibitions are probably of the same essential nature as artificial inhibitions due to anesthesia. In both cases the same kind of physico-chemical modification in the irritable elements appears to form the essential determining condition.

The phenomena of anesthesia have thus the widest biological interest; they belong chiefly in the class of chemical inhibitions or desensitizations. The inverse phenomenon of sensitization—enhancement of irritability or responsiveness—is equally widespread and plays an equally important physiological role. Although its study has received less attention than that of anesthesia, its physiological interest is no less great. Irritability may in fact be altered reversibly either in the direction or increase or decrease.

It is important to note that the same sub-

stance may cause either increase or decrease of irritability or spontaneous activity, according to the conditions of concentration, temperature, or physiological state. In the group of lipoid-solvent substances, which include most anesthetics in common use, weak solutions very generally increase excitability; stronger solutions, within a certain range of concentrations, produce typical reversible narcosis; while still stronger solutions cause cytolysis. The basis common to *all* of these effects requires to be determined. The problem of the general nature of anesthesia is in fact inseparable from the wider problem of the nature and conditions of irritability in general. The essential question may be expressed thus: What is the physico-chemical basis of this property of irritability, and what conditions determine its reversible increase or decrease by chemical or other agents? This problem is among the most fundamental in biology; and the phenomena of artificial anesthesia are of general physiological interest largely because of the light which they throw on this larger problem.

Instances of increase in irritability or spontaneous activity under the influence of low concentrations of anesthetic substances are frequent in both animals and plants. One of the most familiar is the general nervous excitement caused by small doses of ether, alcohol and other narcotics. Automatic rhythmical activity, as of cilia, spermatozoa, or the heart beat, is very generally heightened in weak solutions of alcohol and other narcotics. The nerve-cells controlling the heart beat of Limulus show a faster rhythm in weak solutions of alcohol, chloral hydrate, chloretone, chloroform.[4] Hamburger has shown that many lipoid-soluble substances—iodoform, chloroform, turpentine, benzol, chloral hydrate, camphor, fatty acids, soaps—increase the amœboid and phagocytic activity of leucocytes, while stronger solutions decrease this activity.[3] A similar rule appears to hold for the respiratory center of vertebrates.[4] According to Vernon,[5] weak solutions of narcotics increase the consumption of oxygen in isolated tissues like the kidney. Tashiro and Adams find that low concentrations of urethane and chloral hydrate increase the excitability of nerve as well as its output of carbon dioxid; in higher concentrations both are decreased.[6] The staircase phenomenon in irritable tissues is probably due to the stimulating action of small quantities of substances *fatigue-substances* which in higher concentrations decrease irritability. Small quantities of alcohol increase the responsiveness of voluntary muscle and the energy of its contractions.[7] The musculature of medusae shows increased response to mechanical stimuli in sea water containing a little alcohol.[8] Similar facts are met with in plants. Many depressant substances, when present in low concentration, increase the rate of growth.[9] Traces of ether have an accelerating of *forcing* influence on plant growth, a fact of which practical use is made by horticulturists. Increase in oxygen-consumption under the influence of chloroform and ether has been observed by Elfving and others; higher concentrations decrease oxygen-consumption.[10] Demoor and others have observed an acceleration of protoplasmic rotation in plant cells during the early stages of chloroform and ether narcosis; alcohol also causes this effect.[11] Traces of ether increase the irritability of sensitive plants Mimosa [12]; higher concentrations cause typical anesthesia.[13]

A probably related phenomenon is seen in certain artificial modifications of response induced in various organisms by weak solutions of anesthetics. A striking instance is the reaction of many lower animals to light. Loeb has found that Daphniae, which normally show little or no directive light-response, become positively heliotropic in weak solutions of alcohol and other narcotics, in concentrations of a third to a half of those required for anesthesia.[14] Similarly I have found that the larvae of the marine annelid Arenicola, which normally show strong positive heliotropism, become *negative* in weak solutions of various anesthetics. Similar observations have been made by Torrey, A. R. Moore and other observers.

VITAL PROCESSES SUBJECT TO REVERSIBLE ARREST.

The phenomenon of reversible *decrease* of activity of responsiveness is anesthesia. The vital processes subject to such reversible arrest are of the most varied kind. They include

amœboid movement;[15] protoplasmic rotation in plant cells;[16] all processes depending on response to stimulation, like muscular contraction, and stimulation and conduction in nerve; automatic rhythmical activities like the heart-beat or the motion of cilia or spermatozoa; cell-division;[17] the artificial initiation of development in unfertilized eggs;[18] the stimulating cytolytic or other physiological action of salt solutions;[19] various fermentative and oxidative processes;[20] typical metabolic processes like the assimilation of carbon dioxid by plants;[21] growth processes in plants and animals, and developmental processes dependent on growth and cell-division. It is especially worthy of note that not only motor activity and responsiveness are subject to control of this kind, but also processes like growth and development. The growth of seedlings may be temporarily arrested by ether in sufficient concentration, as Claude Bernard showed.[22] Cell-division in the developing eggs of sea-urchins is checked by anesthetics in concentrations of the same order as those required for neuro-muscular anesthesia in Arenicola larvæ.[23] It is thus not surprising that developmental processes, depending as they do on cell-division and growth, are similarly subject to inhibition by anesthetics. Stockard and McClendon[24] have shown that such substances induce abnormalities like cyclopia in developing fish eggs,—an effect which is to be referred to the arrested development of certain portions of the central nervous system, especially the anterior region of the forebrain between the optic vesicles. Abnormalities of growth and development as well as of irritability may thus be produced under the influence of anesthetics. Since an automatic power of growth—*i. e.*, increase in specifically organized and metabolically active material—is perhaps the most fundamental manifestation of vital activity, the fact that it is subject to reversible arrest by anesthetic substances is of the greatest biological significance and illustrates in a striking manner the unity of the conditions which control the most various cell-processes. We must infer that in the general processes of constructive as well as of destructive metabolism, processes are concerned which are identical with those underlying the ordinary manifestations of stimulation. These latter, however, are almost certainly primarily dependent on surface-changes, of which the most essential are probably variations in the electrical polarization of the plasma-membranes. The controlling influence of membrane-processes in such fundamental physiological activities as growth and assimilation is thus indicated by this susceptibility to arrest by anesthetics.

EXTERNAL CONDITIONS AFFECTING CELL CHANGES.

In any complete theoretical discussion of anesthesia it is necessary first to consider the general conditions under which living cells in general undergo reversible decrease or loss of irritability. This change occurs under a variety of external conditions,—mechanical, thermal, electrical and chemical. Mechanical shock may cause temporary loss of irritability. This is probably an effect of over-stimulation due to prolongation of the refractory period; it resembles in some respects the effects produced in voluntary muscle by poisons like veratrin, which greatly prolong the relaxation-phase and the recovery of irritability following contraction. The paralysis due to mechanical shock is, however, probably different from that of anesthesia; it represents an injury from which the cell can recover, while true unmixed anesthesia is quite without injurious action. Certain effects of altered temperature have a closer resemblance to anesthesia. Most cells and tissues, within the range of temperature in which they show normal activity, show decreased automatic activity with decrease of temperature. Thus according to Snyder[25] the heart of the tortoise shows eighteen beats per minute at 20° and thirty-five at 30°. Observations on the hearts of other animals have given similar results;[26] within the physiological range of temperature the rate is doubled or trebled by a rise of 10°. This rate of change of velocity with temperature, or temperature-coefficient, is characteristic of chemical reactions in general and is not a distinctively physiological phenomenon. Metabolic activity and the dependent vital processes are slowed by cooling just as any chemical process is slowed. The same temperature-coefficient is shown by a large number of physiological processes, including cell-division, rate of conduction in nerve, enzyme-action and

many others.[27] Thus the above effect of cold is due simply to a slowing of chemical reactions in cells and has in it nothing distinctively vital. It is important, however, to consider this effect in relation to the problem of anesthesia, for a simple decrease in reaction-velocity, due to the presence of anti-catalytic substances, is held by various investigators to be the essential condition of anesthesia. Decrease in the rate of a physiological process, like the heart beat, or muscular contraction, or the spread of the excitation-wave in nerve, is not, however, necessarily associated with a change in the irritability and other vital properties of the tissue; in fact moderate cooling may increase the irritability of nerve. Irritability and rate of metabolic processes represent in fact two independent variables. We infer that anesthesia is not simply an expression of a decrease in the velocity of certain chemical reactions, such as oxidations, but that some other factor enters, probably physical in nature. Certain other effects of temperature bear a closer resemblance to true anesthesia. Various irritable tissues become reversibly insensitive at temperatures slightly below or above the normal physiological range. Thus the frog's heart shows an accelerated rate with rise of temperature up to 36° or 37°; it then becomes temporarily inactive and insensitive (heat-standstill), but resumes beating if the temperature is lowered. Similarly the musculature of tropical medusæ becomes irresponsive at 40° and recovers on lowering the temperature.[28] This condition of reversible heat-paralysis has certain suggestive resemblances to anesthesia. Cooling may produce a similar loss of sensibility in cells whose normal temperature is high, such as those of tropical marine animals[29] or warm-blooded vertebrates. Sensory nerve endings and masculine lose sensitivity if cooled sufficiently and recover on warming. In these effects structural alterations due to modification of the colloids of the cells (*gelatin*) are probably concerned; and as will be shown later, there are indications that similar changes form part of the essential basis of true anesthesia. The fact that changes of temperature may thus alter the irritability of the tissue independently of their influence on reaction-velocity as such, is highly important to the general theory of narcosis; and it appears unfavorable to those theories which refer anesthesia to a simple change in the rate of chemical processes like oxidation. Recent experiments by Loeb and Wasteneys[30] on sea-urchin eggs illustrate this: they found that during a condition of narcosis sufficient to arrest cell-division the rate of oxidation was lowered by only 10%; the same effect on the rate of oxidation results from a simple lowering of temperature by 2° to 3°, a change which only slightly retards cell-division. Decrease in the rate of oxidation as such is thus quite insufficient to account for the effect. The fact that in frogs' muscle a lowering of temperatue of 20° (from 35° to 15°) which reduces the rate of oxidation to one-fifth of its former value—leaves irritability unimpaired, indicates that any explanation of anesthesia based on simple decrease in reaction-velocity is inadmissable. A similar decrease in the rate of oxidation can be produced only by concentrations of lipoid-solvent anesthetics much higher than those requisite for anesthesia.

RELATION OF THE CONSTANT ELECTRIC CURRENT TO ANESTHESIA.

The constant electric current produces in many irritable tissues effects closely resembling true anesthesia. Many physiological inhibitions may be caused by passing a constant current through the tissue. There is indeed reason to believe that many of the normal inhibitions, in the neurones of reflex arcs, are electrical in their nature.[31] The anti-stimulating or desensitizing action of the constant current thus deserves careful consideration in any general theory of anesthesia. As is well known, the action of currents on irritable tissues like nerve and muscle is *polar;* where the current enters the tissue there is decreased irritability, depression, or inhibition (anelectrotonus); where it leaves there is excitation or heightened irritability (catelectrotonus). Thus a nerve becomes inexcitable near the anode when the constant current is passed; under similar conditions the heart is inhibited and voluntary muscle relaxed. The condition is reversible, and in fact constitutes a typical local anesthesia. The essential basis of the effect appears to be an altered electrical polarization of the cell-surface. Near the anode, where the current enters the cell or irritable

element, the normal outer positivity of the semi-permeable plasma-membrane is *increased;* apparently this change renders the membrane irresponsive to stimulation. Variations in the electrical polarization of the plasma-membrane are in all probability constantly associated with variations in irritability. The facts of electrotonus show that such changes of polarization may profoundly alter the irritability and automatic activities of the cell. This general conception is of the greatest importance in the theory of anesthesia, and will be reconsidered later.

ANESTHETIC INFLUENCE OF CERTAIN NEUTRAL SALTS.

The most important instances of anesthesia are those produced by chemical substances. First it should be noted that substances belonging to the most various classes may have anesthetic effect. This fact is overlooked in theories like those of Overton and Meyer, Traube, and others, which refer anesthesia to the special properties of lipoid-solvent substances, which are regarded as acting either by dissolving in the lipoid constituents of the cell or by absorption at the surfaces of membranes or other structures. The anesthetic influence of certain neutral salts shows, however, that lipoid-solubility or surface-activity is not essential to narcotic action, magnesium sulphate has long been used by naturalists to narcotize marine animals; more recently it has been applied by Meltzer to produce spinal anesthesia in mammals. Similar reversible depressant effects are produced by potassium salts. Salts of calcium and strontium also cause reversible desensitization of isolated nerve and muscle. In most animals the calcium content of the medium has marked influence on irritability and automatic activity; this is well shown in the case of vertebrate muscle; lowering the ratio of calcium to sodium in indifferent media like Ringer's solution has a sensitizing effect, and if the calcium falls too low the muscle twitches spontaneously; increasing the calcium-sodium ratio has a desenitizing action; these effects are reversible.[32] Calcium also antagonizes the stimulating and sensitizing action of pure solutions of sodium and other salts on muscle and nerve. Similarly the heart beats best in media of a certain calcium-content. In marine medusæ (Rhizostoma according to Bethe) the rhythmical beat ceases when the animal is transferred to calcium-free seawater, and is restored if calcium is added; still further addition of calcium again arrests the movement.[33] These facts make it clear that alteration of the salt-content of the media may have effects essentially identical with anesthesia. This is a fact of much theoretical interests, since it indicates that the general condition of the colloids of the cell, especially of the surface-layer or plasma-membrane, is a chief factor in determining the irritability and automatic activity of the living cell. Further evidence of this will be given later. Modification of the properties of this layer may result from an alteration in the state of either the lipoid or the protein constituents of the plasma-membrane, and if this alteration is reversible a temporary inhibition, or anesthesia, may result. A related condition is seen in the irritable tissues of higher animals, such as muscle and nerve. In these tissues irritability depends on the presence of certain salts in the media; simple withdrawal of salts and replacement by indifferent non-electrolytes like sugar is followed by a temporary loss of irritability; the latter is restored by return to media containing salts, especially sodium salts.[34] The musculature of certain marine animals (Arenicola larvæ) is similarly inactivated in isotonic solutions of non-electrolytes, and regains irritability in isotonic solutions of various neutral salts. Solutions of sodium salts, together with a small proportion of calcium, are especially favorable; sodium may be partly replaced by lithium but not by other metals.[35] Thus the presence of certain salts in the media is necessary for normal irritability,—hence the effects of isotonic sugar solution, which are due to the absence of salts, not to any special action of the non-electrolyte itself. The salt-content of the medium may be reduced to a small fraction—one-tenth or less—of the normal by diluting the physiological salt solution with isotonic sugar solution, without causing loss of irritabilty. But with the complete withdrawal of salts irritability soon disappears. In cases like this, where normal irritability is dependent on the salt-content of the media, modification of the latter may induce a reversible desensiti-

zation closely resembling anesthesia. Probably several factors enter in the production of this effect, of which the two chief are, a direct change in the properties of the plasma-membrane (in its colloidal consistency or electrical polarization), and a lowering of the electrical conductivity of the medium.

The reaction of the media (H-ion concentration) also has profound influence on the irritability and automatic activity of many cells; and a reversible suspension of function akin to anesthesia may result from a slight change in this reaction. In higher animals the normal reaction of blood-plasma is not far from neutral, and varies only slightly from a constant normal (C_H=0.35×10^{-7} to 0.5×10^{-7}); but certain cells of the central nervous system are especially sensitive to such variations. The activity of the respiratory center appears to be regulated by variations in the H-ion concentration of the blood, cessation of activity resulting from a slight decrease (increased alkalinity), and increased activity from a slight increase.[36] Reversible cessation of activity may thus result from a slight change in reaction, due to loss of CO_2. Similar conditions are known to exist in certain marine animals; thus according to Bethe,[37] slight increase in the alkalinity of the sea water arrests, while slight acidulation accelerates, the rhythmical contraction of medusæ. On the other hand, the activity of many cells and tissues is favored by slight increase in external alkalinity, and depressed by slight acidulation. The irritability and automaticity of living cells are thus largely a function of the reaction, and this fact has an intimate bearing on the question of the mechanism of anesthetic and other inhibitions. The precise physico-chemical basis of this action is uncertain but probably depends chiefly on alterations in the electrical polarization of the cell-surface. Slight variations in alkalinity or acidity are known to produce marked effects on the electrical polarization of surfaces bathed by media of approximately neutral reaction.[38]

ANESTHETIC EFFECTS OF LIPOID-SOLVENTS.

The chief chemical substances exerting a reversible depressent influence on a wide range of vital activities are those numerous and chemically diverse organic compounds of which the most evident common property is a solvent action on, or solubility in, fats and fat-solvents. Substances of this class form the majority of anesthetics in common use; they include alcohols, ethers, esters, aldehydes, ketones, nitriles, amides, various normal and substituted hydrocarbons (chloroform, benzol) and other related compounds. Most of these bodies are members of homologous series; and it is highly characteristic of such series that the ratio of oil-solubility to water-solubility (oil-water partition-coefficient) increases regularly with increase in molecular weight. At the same time the narcotizing power increases; —i. e. in any single series (alcohols) the higher the molecular weight the lower the concentration required for narcosis. It was this general parallelism that led Overton and Meyer to the view that anesthetic power, in the case of any substance, is a direct function of its solubility in the fat-like or lipoid constituents of the cell. That a connection exists between the fat-solvent and the anesthetic properties of a compound had previously been suggested by Bibra and Harless in 1847, and the same view was later expressed by Hermann, Claude Bernard, Richet, Ehrlich and others.[39] The first systematic studies of this relationship were, however, those of Overton and Meyer, the results of whose experiments, carried on independently, were published about the same time (1899).

In a study of the permeability of animal and plant cells to various types of compounds Overton[40] had reached the conclusion that solubility in lipoids was the chief factor determining the ready entrance of a compound into cells; compounds with well-marked power of penetration belonged chiefly to the narcotic group; and in a later extensive investigation on narcosis in tadpoles[41] a far-reaching parallelism was found between the oil-water partition-coefficients of a wide range of organic compounds and their narcotizing action. The nature of Overton's results may be best seen from the following series, which gives the concentrations required to narcotize tadpoles in the case of the ethyl esters of the first five fatty acids, as shown in Table 1.

TABLE I.

Ester	Narcotising concentration (mols per liter)	Solubility in Oil and Water
Ethyl formate	0.07m—.09m	oil: water=4:1
" acetate	.03m	in 15.2 parts water; in all parts oil
" propionate	.01m—.012m	" 50 " " " " " "
" butyrate	.0043m	" 190 " " " " " "
(" isobutyrate)	.0057m	" 140 " " " " " "
" valerianate	.0019m	" 500 " " " " " "

The narcotic action is seen to increase steadily with decrease in water-solubility,—i. e. increase in the ratio of partition between oil and water. Each member of the series is from two to three times as effective as its immediate predecessor. This rule appears to hold very generally for members of homologous series, and a large number of similar instances have been collected by Traube and other recent investigators.[42] Numerous other experiments with alcohols, hydrocarbons, aldehydes, and ketones, showed a similar increase in narcotic action with increase in oil-water partition-coefficient. Overton accordingly drew the conclusion that narcotics act by dissolving in certain substances, contained especially in nerve cells, which resemble fats in their solvent properties; these substances are the lipoids, especially lecithin and cholesterin, which appear to be essential constituents of protoplasm; it is the physical modification of these substances, due to their being charged or impregnated with the lipoid-soluble narcotic, that forms the essential condition of anesthesia. Meyer's conclusion was similar;[43] the narcotizability of cells is thus related to the nature and the proportion of the lipoids present in the protoplasm; the high susceptibility of nerve-cells is probably dependent on their high lipoid-content. The unequal action of different narcotics depends on their respective partition-coefficients, which determine their distribution in a mixture of water and lipoid substances. The greater the relative lipoid-solubility, the larger the proportion of the anesthetic present in solution in the lipoid cell-constituents when the partition-equilibrium is reached. Hence if the lipoid-solubility of a substance is very high, extremely dilute solutions may exert anesthetic action. Overton, for example, found that phenanthrene could narcotize tadpoles in dilutions so low as one part in 1,500,000 of water.

Overton's studies of permeability had led him to the conclusion that the outer layer or plasma-membrane of cells consists largely of lipoid material; in this way he explained the ready entrance of lipoid-soluble substances into cells. Now it is an evident corollary of Overton's hypothesis that if the anesthetic acts by changing the physical state of the lipoid cell-constituents it must affect the properties of a lipoid-rich cell-structure like the plasma-membrane. Overton, however, does not refer narcotic action specifically to a modification of the plasma-membrane alone, but to a general modification in the physical state of the cell-lipoids wherever situated. Recently, however, much evidence has accumulated indicating that the essential influence is that exerted on the plasma-membrane, and that it is the modifications in the properties of this structure which determine the characteristic anesthetic effect. This evidence and its implications will be considered later.

The hypothesis of Overton and Meyer has received wide acceptance. It is not clear, however, why simple solution of chemically indifferent substances in the lipoids of the tissue should so modify its irritability; and Overton and Meyer do not attempt to explain this connection. The parallelism between lipoid-solubility and narcotic action is not an exact one, and many exceptions to the rule are known. The powerful narcotic action of chloral hydrate, which is several times more soluble in water than in oil, is not thus explained; and lipoid-insoluble neutral salts of magnesium and other metals may exert typical narcotic action. Evidently other factors than solubility may enter. Yet the evidence adduced by Overton and Meyer, as well as by more recent investigators, leaves no doubt that in the case of organic anesthetics high lipoid-solubility is typically associated with marked narcotic ac-

tion. The reversibility of anesthesia corresponds to the reversibility of the process of solution. On this view the chemical indifference of many anesthetics is not surprising, since the substance acts not by chemical combination but by simple solution in the cell-lipoids.

According to Overton and Meyer's hypothesis, it is the *solution* of the narcotic in the lipoid which determines anesthetic action. This view has recently been attacked from various sides. Thus, according to Traube,[44] the anesthetic acts not by *dissolving* in the cell-lipoids, but rather by undergoing surface-condensation or adsorption at the physiologically active surfaces, within the living system; these may be the surfaces of special cell-structures, or of colloidal particles, whether lipoid or protein. The catalytic activity of these surfaces is thus decreased, and the reaction-velocities of essential chemical processes, especially oxidations, is lowered; a corresponding depression of cell-functions results. Whether this effect is to be attributed to a displacement of metabolically active water-soluble substances like sugar, whose surface-activity is relatively small, or to a direct alteration in the catalytic properties of the physiologically active surfaces themselves, is uncertain.

THE ESSENTIAL FEATURES OF TRAUBE'S VIEWS.

The essential feature of Traube's view is that it regards the surface-activity of a narcotic compound, i. e. its influence in lowering surface-tension—rather than its lipoid-solubility—as the determining factor in its depressant action. This surface-activity determines the degree of adsorption and hence indirectly the degree of anesthetic action. It is well known that the surface-tension of such a solvent as water, in contact with air or with another liquid or a solid, is greatly influenced by the presence of dissolved substances. This influence is usually in the direction of a decrease. A few substances like inorganic salts and sugars increase the surface-tension of water, although the effect is slight; but the majority, especially of organic substances, cause well marked and often great decrease of surface-tension. This is especially true of substances whose water-solubility is limited; and in general the more soluble a substance is in oils or other water-insoluble organic solvents and the less soluble in water, the greater its influence, (for a given molecular concentration) on the surface-tension of water. In a capillary tube the level of pure water or of an aqueous solution is raised, by means of the contractile force or tension of the surface of the water-film lining the walls of the tube, to a certain height above the level of the water outside. This height, (h), is proportional to the surface tension of the water (s), and inversely proportional to the radius of the tube (r) and the specific gravity (g) of the liquid ($h = \frac{2s}{rg}$). The relative surface-tensions of aqueous solutions may thus be determined by measuring the heights to which the column of solution is raised by capillarity in a given tube. This height is decreased by surface-active substances, and the degree of capillary activity or tension-lowering action of different substances can thus be determined. Now in any homologus series this action (for equimolecular solutions) is found to decrease as the molecular weight increases. The surface-tension in milligrams per linear centimeter (i. e. the pull exerted by a strip of surface one centimeter wide) of m-4 solutions of the first five aliphatic alcohols at 15° is given by Traube as follows; the surface-tension of the m-4 solution of dextrose, a physiologically important surface-inactive compound, is given for comparison, in Table II.

The second column gives the concentrations required to effect a definite lowering of surface-tension. It will be observed that the surface-activity of each member (as measured by the reciprocals of the isocapillary concentrations) is approximately a third of that of its immediate predecessor. The third column shows that narcotic activity increases from each member to the next following in a closely similar proportion. Results of this kind are on the whole typical for homologous series. The question arises as to their general physiological significence.

According to Traube the essential physico-chemical factor in these physiological effects is the characteristic influence which surface-tension has upon the distribution of dissolved substances in any polyphasic system. The general

TABLE II.

Liquid (solutions—m-4)	Surface-tension (milligrams per centimeter)	Molecular concentrations of isocapillary solutions	Concentrations for Narcosis of Tadpoles (Overton)
water	73		
m-4 dextrose	73.3		
methyl alcohol	70.5	14.0	0.52m—0.62m
ethyl "	67.3	5.0	0.27m—0.31m
n-propyl "	58.9	1.6	0.11m
i-butyl "	44.9	0.46	0.045m
i-amyl "	30.5	0.14	0.023m

principle of Willard Gibbs and J. J. Thomson states that substances which lower the surface-tension of any solvent attain when equilibrium is reached a higher concentration in the surface-layer than in the interior of the solvent; a surface-condensation or adsorption thus results, which is the greater the greater the surface-activity of the dissolved compound. Hence substances having a high degree of surface-activity are as a class readily adsorbed. The effect is the same as if a relatively slight coherence existed between the solvent and the dissolved substance. Hence Traube conceives of a surface-active substance as one in which the union or adhesion between solute and solvent is slight. That is, relatively little work is required to separate the substance from solution; and he has introduced the expression *Haftdruck* (adhesion-tension or solution-affinity) to designate this condition. The capilliary activity of any substance in a given solvent varies inversely with its solution-affinity (*Haftdruck*) relatively to that solvent. The lower the solution-affinity relatively to water the greater is the tendency of any substance to pass out of its solution in water; this tendency favors the entrance of capillary-active substances into other adjoining solvents or media, *e. g.* into and through the membrane bounding cells.[45] The ready penetration of such substances into living cells is in fact referred by Traube not to lipoid-solubility but to low solution-affinity in relation to the medium bathing the cell. A tendency to surface-condensation or adsorption is a characteristic accompaniment of low solution-affinity to water; the marked physiological activity shown by surface-active substances as a class is a direct consequence of this tendency.

According to the data already cited the narcotic activity of organic substances shows a parallelism between both capillary activity and lipoid-solubility. Other physiological effects (membrane-formation in sea-urchin eggs,[46] reversal of the sense of heliotropism, sensitizing action, cytolytic action) show a similar parallelism. The question of whether the particular physiological effect under consideration is determined by one or the other factor or by the interaction of both has to be decided by further evidence. In favor of the view that lipoid-solubility rather than surface-activity is the essential determining factor in the action of lipoid-soluble narcotics is the fact that the action varies with temperature in the same direction as the oil-water partition-coefficient. This is shown in a remarkable manner in the following table from Hans Meyer.[47] The concentrations required to narcotize tadpoles were determined at the two temperatures 3° and 30° using (a) narcotics whose relative solubility in oil *decreases* with rise in temperature, and (b) those in which it *increases*. The critical anesthetizing concentrations for the following six anesthetics are given in Table III.

In the first three compounds the relative lipoid-solubility decreases and the narcotizing concentration increases with rise of temperature; while with the others the conditions are reversed. Thus simple cooling suffices to restore activity to tadpoles anesthetized in chloral hydrate at 30°. If adsorption under the influence of surface-tension were the main factor in these effects, such a change of narcotic power with temperature would be inexplicable, since surface-tension is influenced in a totally different manner by change of temperature. The fact that anesthetics collect in cells

TABLE III.

Anesthetic	Critical Concentration for Anesthesia		Oil-Water Partition-coefficients	
	at 3°	at 30°	at 3°	at 30°
A. Salicylamide	m–1300	m–600	22.232	14.00
benzamide	m–500	m–200	0.672	0.437
monoacetin	m–90	m–70	0.099	0.066
B. ethyl alcohol	m–3	m–7	0.026	0.047
chloral hydrate	m–50	m–250	0.053	0.236
acetone	m–3	m–7	0.146	0.235

in higher concentration than in the medium, while not decisive, also appears to favor the partition rather than the adsorption theory of narcosis. Chloroform, ether and esters undergo concentration in nervous and other tissues, as Pohl[48] and Hedin[49] have shown. Warburg and Wiesel[50] have also found that in the case of yeast the tendency of compounds to concentrate in cells increases with increase in their narcotic power. In solutions that diminished fermentative activity by one half, phenyl urethane was found to be three times and thymol nine times more concentrated in the cells than in the medium. This strongly suggests a distribution according to relative solubilities.

What Traube especially insists upon is that effects similar to narcosis are shown in cases where lipoid-solubility can play no part. Thus according to Warburg and Wiesel,[51] the fermentative and oxidative activities shown by lipoid-free preparations of dried microorganisms are influenced by the lipoid-solvent anesthetics in the same manner as in the intact organisms. It is to be noted, however, that the effective concentrations are much higher in the case of such preparations than in that of living cells. Traube cites a large number of observations made with solutions of various surface-active substances showing that with both animal and plant cells, as well as with enzymes, the degree of narcotic and cytolytic action—of inhibition and destruction in the case of enzymes—is nearly proportional to the surface-activity of the solution.[52] Solutions of widely different substances, provided they have the same surface-tension (*isocapillary solutions*), have equal physiological action. In the following table I have collected observations showing a number of different physiological effects produced in various organisms by members of the aliphatic alcohol series. In each instance the molecular concentrations required to produce a definite physiological effect are given; the molecular concentrations which cause equal lowering of surface-tension (*isocapillary concentrations*) are given in the last horizontal column of Table IV.

These data show that the increase of surface-activity observed on passing from one member of the series to the next is very generally associated with a proportionately similar increase of physiological activity. In general each member has from two to three times the capillary activity of its immediate predecessor; and the same holds true for its physiological activity. It is to be noted, however, that it also holds true for lipoid-solubility.

If physiological activity is in fact a function of capillary activity, solutions of equal surface-tension ought to exhibit equal narcotic or other physiological effects. Traube cites various observations indicating that this is frequently the case. Thus Czapek[65] has determined for a large number of organic substances the surface-tensions of the solutions which have equal effects in liberating tannin from plant cells (the leaves of Echeveria); this effect is analogous to hemolysis and depends on increase in the permeability of the plasma-membrane. The surface-tensions of equally effective solutions (against air) were found to approach a fairly constant value,—about two-thirds of that of pure water. Kish[66] also found that isocapillary solutions had equal effects in preventing germination of yeast; and H. Zuckerkandl[67] obtained similar though less

TABLE IV.

Physiological Effect	Producing Effect. Concentrations of Alcohols (mols per litre) for							
	methyl	ethyl	propyl	butyl	amyl	hexyl	heptyl	octyl
Narcosis of Tadpoles (Overton)[53]	0.57	0.29	0.11	0.338	0.023			.0004
Narcosis of Arenicola Larvæ[54]	2.2	1.1	0.34	0.09	0.03			.001
Prevention of Cleavage in Arbacia Eggs[55]		0.87	0.27	0.086	0.037			.001
Checking of Development in Strongly locentrotus Eggs (Fühner)[56]	0.72	0.41	0.136	0.045			0.0017	.0005
Narcosis of Daphnia (Loeb)[57]	1.2	0.6	0.2	0.12	0.04			
Production of Heliotropism in Daphnia (Loeb)[57]	0.6	0.2	0.05–0.1	.04				
Hemolysis (Fühner and Neubauer)[58]	7.34	3.24	1.08	0.318	0.091	0.034	0.012	0.004
Decreasing Oxidations by 50% in Blood-corpuscles (Warburg)[59]	5.0	1.6	0.8	0.15	0.045			
Inhibition of Fermentation by ether-extracted yeast (Warburg)[60]	5.0	3.5	1.3	0.54	0.23			
Depression of Isolated Tortoise Ventricle by 50% (Vernon)[61]	1.1	0.53	0.23	0.05	0.02			
Destruction of Indophenol Oxidase (Vernon)[62]	10.5–14	4.8–8	1.5–2.75	0.32–.09				
Precipitation of Nucleo-proteid of Liver (Battelli and Stern)[63]	5.7	2.38	1.12	0.45	0.21			
Destruction of Oxydon of ox-muscle (Battelli and Stern)[63]	7.54	3.57	1.16	0.44	0.19			
30% Decrease in Action of Yeast Invertase (Meyerhof)[64]	3.0	1.3	0.5	0.27	0.21			
Concentrations of Isocapillary Solutions	14.0	5.0	1.6	0.46	0.14			

uniform results for the inhibition of protoplasmic streaming in plant cells. The results of observations by Fuhner and Neubauer and also by Traube himself on hemolysis are similar. Thus, taking again the series of alcohols: the surface-tensions of the least concentrated solutions which free tannin from Echeveria leaves and which inhibit the germination of yeast cells are as follows: (water—1) as shown in Table V.

In each instance equal physiological effects are produced by solutions of approximately equal surface-tension. Czapek finds that the same rule of equal action for isocapillary solutions holds good for ketones, esters, urethanes, and other compounds. Lately, however, Vernon,[68] Höber,[69] and others have pointed out various exceptions to this rule; thus chloroform, chloral hydrate, nitromethane, and ethylene glycol begin to free tan-

TABLE V.

Alcohol	Critical Surface-tensions of Solutions Causing	
	A. Exosmosis of Tannin from Echeveria Cells	B. Inhibition of Growth of Yeast
methyl	0.7	0.51
ethyl	0.67	0.48
n-propyl	0.675	ca. 0.49
i-propyl	0.69	—
n-butyl	0.69	—
i-butyl	0.665	ca. 0.495
i-anyl	0.665	0.49

nin from Echeveria leaves in solutions of much higher surface-tensions than the above. And with the higher alcohols the surface-tensions of the effective solutions are lower than the theory requires. These deviations from the rule of isocapillarity are referred by Traube partly to chemical influences (e. g., presence of acid in chloral hydrate solutions), partly to incorrect determination of surface-tension in solutions of volatile substances like chloroform and ether, partly to the influence of viscosity. In general it appears that the more viscous compounds, (the higher alcohols) show equal physiological action, e. g. hemolysis, in solutions of lower surface-tension than Traube's theory demands; Traube, however, believes that this difference is due simply to slowness of penetration incident to the high viscosity of the adsorbed layer of the narcotic at the surfaces of red corpuscles, where the essential action takes place. For solutions of approximately equal viscosity the rule of equal action with equal capillarity appears to hold true. In general isocapillary solutions of surface-active substances have less hemolytic or other physiological action the greater their viscosity; hence equal action for isocapillary solutions is to be expected only when the viscosities are similar.[70] Even this, however, is not always the case. For instance, Loeb[71] has found that weak solutions of fatty acids, as well as weak solutions of narcotics, produce positive heliotropism in daphnids; the least effective concentrations for the first six members of the acid series were: .006n formic, .006n acetic, .005n propionic, .004n butyric, .004n valerianic, .002n caproic. The increase in effectiveness with increasing molecular weight is much more gradual than the increase in capillary activity. The influence of the H-ion concentration enters here and probably constitutes the prepondent factor. The part played by purely chemical action seems to be underestimated in Traube's theory. Where this factor enters surface-activity may be of subordinate importance. Thus, in the case of neutral salts, solutions of equal surface-tensions may have entirely different action on colloids and hence on living cells. Traube's rule is at best an approximation; its significance, however, is not to be underestimated on this account. Adsorption and surface-condensation undoubtedly run parallel with capillary activity; this is a matter not only of deduction from the Gibbs-Thomson principle, but also of direct observation; and surface-forces play so large a part in biological processes that it is not surprising to find a frequent parallelism between the physiological effects of solutions and their surface-activity.

Traube in fact recognizes that the lipoid-content of cells may have an influence on the rapidity of intake of the narcotic—since lipoid-solubility will naturally favor penetration,—and hence may be a factor in the narcotic action; but the narcosis itself does not depend on this solution in lipoids; "the lipoid-content influences narcotic action, but does not determine it; even lipoid-free cells may be narcotized."[72] This conception, however, does not seem adequate in view of the observations of Meyer, cited above, on variation of narcotic action with temperature.

It is important to note that surface-active substances affect not only biological processes, but also catalysers of various kinds, especially those due to enzymes and other colloidal catalysers (platinum, etc.), where the action is probably dependent on the character and extent of the surface between catalytic agent and medium (heterogeneous catalyses). Enzymes are colloidal catalysers formed in cell-metabolism; as colloids it is to be expected that surface-conditions will largely influence their action. Recently Bayliss[73] has emphasized the importance of such conditions. He has shown that various enzymes (lipase, emulsion, urease, trypsin) retain their activity when suspended in media in which they are insoluble. This fact is best explained on the

view that increased concentration of the substrate at the surface of the enzyme is mainly responsible for the increased reaction-velocity in its presence. This view does not explain specificity, which is probably a matter in which selective absorption and stereochemical conditions enter as factors; but it leads to the general expectation that readily adsorbable, *i. e.* surface-active, substances will as a class have marked influence on enzyme-action.

In many organisms oxidations are the chemical processes which are most evidently influenced by narcotics; and the view that narcotic action consists essentially in a suppression of oxidation has gained wide favor, and has been supported chiefly by Verworn in Germany, and by Mathews, Loevenhart and others in America. The view that this anti-oxidative action may be exerted directly upon the oxygen-catalysers of the cell is supported by Traube. Considerable evidence consists favorable to this view. Thus Warburg finds that organic iron salts accelerate oxidations in disintegrated sea-urchin eggs, and he further finds that this accelerative action is checked by urethane.[74] This interesting observation suggests the possibility that catalysis by iron plays a part in intracellular oxidations; this catalysis is checked by anesthetics, and it is to be inferred that oxidative processes under the influence of organic catalysers or oxidases would be similarly effected. In support of this conception Traube cites various instances where oxidative processes are checked by surface-active or narcotic substances.[75] Such instances include the decomposition of hydrogen peroxid by platinum (Bredig); the oxidation of sodium sulphite by free oxygen (Bigelow, Titoff, Young); Young finds this process checked by traces of morphin, brucin, nicotin, and especially quinin; and Traube even refers the antipyretic action of quinin to its inhibiting action on oxidation; the oxidation of phosphorus and phosphorus trioxid by free oxygen (Centnerszwer, Scharff); oxidation of stannous chlorid (Young); oxidation by tissue oxidases (Vernon, Baer and Meyerstein); catalytic oxidation of oxalic acid by animal charcoal (Warburg[76]). Thus not only oxidations under the influence of heterogeneous or colloidal catalysers may be checked by surface-active substances, but also oxidations in homogeneous solution. This would indicate that surface-activity is not the only factor involved. On the basis of these and other facts Traube puts forward the hypothesis that narcotics are essentially negative catalysers, especially in relation to oxidative processes.[77] The question of how this anti-oxidative effect is produced within the living cell is the essential one. Traube and others have suggested that the direct action of surface-active and narcotic substances on colloids may be a chief factor. Moore and Roaf[78] have investigated the precipitation of serum by such substances, an effect which shows a general increase with surface-activity. These authors, however, refer the effect to the formation of loose chemical combinations between the narcotic and the proteins; the quantity of chloroform and other anesthetics dissolved by serum is several times greater than by water; they regard the excess as held by chemical union, and they attribute narcotic action to such loose protein-anesthetic compounds *"which limit the chemical activities of the protoplasm,"* including presumably the oxidations. Warburg and Wiesel also find that narcotic substances have a precipitating action on the press-juice of yeast, and that the anti-fermentative action runs parallel with the precipitating action; and they recall the older view of Claude Bernard according to which a semi-coagulation of the cell colloids forms the basis of narcosis.[79] Battelli and Stern[80] find that the nucleo-proteins of cell extracts are also precipitated by lipoid-solvent anesthetics, and that the precipitating action runs parallel with the influence in checking the activity of cell-oxidases or oxydones. Traube also cites observations by Sshryver[81] in support of this general point of view; surface-active substances retard the gelation of certain colloidal solutions, e. g. of sodium cholate under the influence of calcium salts, and the degree of retardation runs parallel to capillary activity and narcotic action. Physical alterations of the cell-colloids may thus lie at the basis of the anti-oxidative action which, according to this view, conditions the narcotic action. Other instances of this effect will be considered later. Traube expresses his essential view as follows: "the physical alterations of the cell colloids—and by no means of the lipoids alone—form one of the

most essential conditions for the slowing of chemical processes in cells, and hence also for narcotic and other toxicological processes. These physical alterations are a consequence of the depressant influence which narcotics exert upon surface-tension, and upon the internal pressure of the cell contents.[82] According to this conception the physical alteration of the colloids would be the primary effect of the narcotic, and decrease of oxidation secondary; this view is more consistent with the membrane-theory of narcosis about to be described than with the previously quoted view which refers narcosis to a direct anti-catalytic action. According to the membrane-theory it is the plasma-membrane which is primarily affected, and the decrease of oxidations (when this occurs) is a secondary consequence of the change in the membrane. This view would make the direct action of the anesthetic on oxidation-processes relatively unimportant. To regard anesthesia as dependent on a direct anti-catalytic action seems insufficient, especially in view of the fact that the effective anti-catalytic concentrations are so much higher than those required for narcosis. It should also be remembered that magnesium sulphate and other salts can act as anesthetics —such salts have no such direct anti-catalytic action—also that the electric current may show the same influence. The action of anesthetics on oxidases will shortly be considered in more detail.

AGGREGATION OF COLLOIDS IN RELATION TO THE GENERAL THEORY OF ANESTHESIA.

The general fact that surface-active substances alter the physical condition or state of aggregation of many colloids is, however, highly important to any general theory of anesthesia. Probably this effect is to be related to their influence on the electrical potential-difference normally existing between the collodial particles and the medium. Gouy[83] found that the potential-difference between mercury and sulphuric acid in the capillary electrometer is lowered by the presence of many surface-active and narcotic substances; similar observations were made by Abl[84] for cadmium alamagam cells, and by Grumbach[85] for various contact potentials; and according to Traube the order of relative action in all of these cases is essentially that of capillary activity. Now precipitation or increased aggregation of colloids is typically associated with decrease in the electrical polarization of the colloidal particles; and capillary-active substances which produce this latter effect ought therefore to further such precipitation. A similar influence of anesthetics on the potentials shown by organic membranes like apple-skin against salt-solutions was also observed by Loeb and Beutner;[86] the concentrations required for appreciable lowering of potentials were, however, much higher than those ordinarily required for anesthesia. Notwithstanding this difficulty Traube suggests that a decrease in contact-potentials, as well as of surface-tension at the active surfaces in tissues like nerve, may be an important factor in the action of narcotics. To quote from Traube's recent paper on narcosis: *"the narcotic substances, in collecting at the boundary-surfaces of cell-wall and cell-fluid, lower there the electrical contact-potentials, and in so doing directly prevent the transmission of motor and sensory impulses by means of nerve centers. . . . . This retarding or inhibiting influence, exerted by substances of low solution-affinity (Haftdruck) to water, upon the oxidations and other intracellular processes conditioned by cell-colloids, and also upon the electrical phenomena at boundary-surfaces, is the cause of that condition which we designate as narcosis."*[87] A somewhat similar view had previously been expressed by A. B. Macallum: *"chloroform, ether, alcohol, and chloral lower surface-tension in aqueous solutions, in blood plasma and lymph, and, in all probability also, the surface-tension of all cells, but especially of the nerve-cells. This would make them incapable of receiving or transmitting a nerve-impulse."*[88]

THE PHENOMENA OF ASPHYXIA AND DEOXIDATION IN RELATION TO ANESTHESIA

The general view that narcosis is essentially a phenomenon of asphyxia or retarded oxidation is an old one, suggested by Claude Bernard and others, and has been revived in somewhat different form of recent years, chiefly through the influence of Verworn and his pupils[89] Decrease in oxidations is in fact frequently observed during narcosis. Thus Alexander and Cserna[90] showed by direct analyses of

blood a marked decrease in the oxygen-consumption of the brain during ether and morphine narcosis; oxidation-processes in the liver are also described under the influence of various narcotics.[91] But whether this decrease is simply a consequence of a paralysis of metabolic as well as of other functions, or whether it is the primary and determinative condition, is a question which has been answered differently by different investigators. Verworn has identified narcosis with asphyxia chiefly because of certain similarities between the physiological behavior of asphyxiated and narcotized tissues and cells. A summation of the effects of narcosis and of asphyxia is seen under certain conditions; thus Winterstein found that frogs asphyxiated by perfusion with oxygen-free salt-solution until reflex activity was lost showed no recovery from the asphyxia if supplied with oxygen while still in a state of anesthesia.[92] The condition of narcosis appears to render oxygen unavailable to the cells. Fröhlich[93] found the same rule to hold for nerve-trunks; normally oxygen revives irritability lost in an oxygen-free medium (nitrogen atmosphere); but oxygen has no such effect on narcotized nerves; similar observations were made by Nagai[94] on ciliated epithelium. There is thus no recovery from asphyxia during narcosis, even with a good supply of oxygen. Nerves subjected to prolonged narcosis show the same physiological changes as after exposure to lack of oxygen (Fröhlich,[95] Boruttan[96]); the rate of conduction is slowed, the refractory period is prolonged, and repeated stimulation causes definite fatigue-effects; oxygen then restores the normal properties, but only in the absence of the anesthetic. All of the phenomena of asphyxia appear during narcosis even in the presence of a good supply of oxygen,—just as they do in an oxygen-free atmosphere in the absence of the narcotic (Frohlich, Bondy,[97] Heaton.[98]) Experiments by Ishikwa[99] on amœbæ gave analogous results; recovery from the inhibited or non-irritable condition, whether due to simple lack of oxygen or to the presence of a narcotic, requires the same condition, namely the presence of free oxygen. Other forms of inhibition, such as the heat-paralysis of the frog's central nervous system, are promoted both by lack of oxygen and presence of narcotics (Winterstein[100]); *i. e.,* anesthesia acts in the same direction as lack of oxygen,—an indication that both conditions produce essentially the same physiological effect. Mansfeld[101] found that in the absence of oxygen tadpoles succumb more rapidly to anesthesia than in its presence; the same is true of simple protoplasmic streaming in plant cells at temperatures of 30° and over (Zuckerkandl).[102] All of these facts seem to indicate that lack of oxygen produces essentially the same effects as anesthesia; that the two actions are largely interchangeable, and hence capable of summation.

In general, however, it may be said in criticism of such conclusions, that inhabitation or prevention under the influences of narcotics, of physiological processes which require oxygen, does not demonstrate that narcotics act directly and primarily upon oxidation-processes. The proper inference is rather that vital processes, *including* those which require free oxygen, are inhibited during anesthesia. But anesthesia may also inhibit physiological processes which are independent of free oxygen, as Winterstein has shown in his experiments on the narcosis of anaërobic animals like Ascaris.[103] Similarly the growth of yeast under anaërobic conditions is checked by anesthetics in the same manner as in the presence of oxygen;[104] and the nerve cord of Limulus, which continues to send out impulses in the absence of free oxygen, is anesthetized by ether in a typical manner.[105] Some more general condition which determines the rate of oxidations, as well as of other metabolic processes and cell-activities, is more probably the one directly affected during anesthesia. This latter view would regard the suppression of oxidations as seconday rather than primary,—an effect rather than a cause of narcosis. During anesthesia those processes which are directly dependent on oxidations are arrested, together with those not so dependent.

Various attempts have been made to refer narcosis to a decrease in the external supply of oxygen, or to an inability of oxygen to enter the cells. Thus anesthesia as well as sleep were at one time popularly attributed to a condition of cerebral anemia,—an obviously untenable view, since neither condition is confined to animals with brain and circula-

tion. That the anesthetic hinders the entrance of oxygen into cells has recently been suggested by Mansfeld;[106] the solubility of oxygen in the lipoids of the plasma-membrane—and hence its rate of entrance into cells—was held to be diminished by the solution of lipoid-solvents in the lipoids; and E. Hamburger[107] attempted to show that narcotic substances actually decreased the solubility of oxygen in lipoids. These views, however, must be regarded as unfounded (see Winterstein's criticism[108]).

The facts which offer best support to the oxidation-theory of narcosis appear to be those which demonstrate an actual decrease in oxygen-consumption by isolated cells and tissues under the influence of narcotics. Thus Warburg and his associates have shown that oxygen-consumption by living cells, of various kinds (red blood corpuscles, sea-urchin eggs, bacteria, liver cells, yeast cells, the central nervous system) is decreased by various anesthetics[109]; and the different narcotic compounds show the same order of relative action as in anesthesia. For example the several alcohols lower the oxygen-consumption of birds' erythrocytes by 50 per cent. in solutions of the following concentrations[110], as shown in Table VI.

TABLE VI.

Alcohol	Concentration of Solution depressing Oxidations 50%		Concentration for Anesthesia of Tadpoles (Overton)
	per cent. (by weight)	Molecular	
methyl	16	5m	0.52–0.62m
ethyl	7.3	1.6m	0.27–0.31m
propyl	5.	0.8m	0.11m
n–butyl	1.1	0.15m	0.038m
i-butyl	1.1	0.15m	0.045m
amyl	0.4	0.045m	0.023m

It is to be noted that these concentrations are much higher than those usually required for anesthesia, as comparison with Overton's results (third column) will show. Vernon also found that anesthetics decreased the oxidation of the indophenol reagent by fresh tissues. An especially interesting fact is that anesthesia causes a similar though less marked decrease in oxidation by dead cells and by tissue-extracts, as has been demonstrated by both Warburg and Vernon.[111] This suggests that the anesthetic influence is exerted directly upon the oxygen-catalysers of the cell; and recently a number of investigators have devoted special study to the inhibiting action of anesthetics on oxidases.

Vernon[112] has investigated the influence of various anesthetics upon the activity of the indophenol-oxidase of the vertebrate kidney. Enzymes which accelerate the oxidative formation of the blue dye, indophenol, from a mixture of d-naphthol and para-diamino-benzene are widely distributed in organisms; and Vernon's investigations on the distribution of this oxidase in the tissues of vertebrates indicate that a relation exists between the oxidase-content of a tissue and its general oxidative activity.[113] Various anesthetics were found to decrease the oxidation, and eventually to destroy the oxidase. The concentrations required to decrease activity by one-half under otherwise constant conditions showed a close parallelism with those required to hemolyze red corpuscles. In both cases the order of relative action was the same as for anesthesia. The parallelism of lipoid-solubility with narcotic action appeared closer than that of surface-activity; and Vernon inclines to the belief that the narcotics exert their action chiefly by dissolving in the lipoids of the plasma-membrane and so altering the properties of this structure, (possibly by interfering with the interaction of oxidase and peroxidase[114]). The oxidase-inhibiting concentrations are, however, far higher than the narcotizing, and correspond rather with the cytolytic concentrations, so that a direct connection seems doubtful. The work of Battelli and Stern[115] on the influence of anesthetics on other tissue oxidases (e. g. a liver-oxidase which oxidizes succinic to malic acid) shows in general similar relations; in this case the inhibiting action was found to run closely parallel with surface-activity,—more so, according to Battelli and Stern, than with lipoid-solubility. It showed also a striking parallelism with a precipitating action on the nucleo-proteids of the tissue. As already stated, a similar precipitating action of anesthetics has been studied by Moore and Roaf,[116] who agree with Battelli and Stern in regarding this action as an important factor in anesthesia; the authors also agree in

attributing the action of anesthetics not to their influence on lipoids alone, but rather to an alteration of the proteins of the tissue. It seems clear that anesthetics may directly inhibit oxidation-catalysis in tissues. But the objection again rises that the concentrations required for these effects greatly exceed those required for anesthesia in living cells.

The relation of oxidases to cell-respiration is still obscure. Present opinion inclines to the belief that these bodies are essentially peroxid-forming compounds (oxygenases) which are activated by other accessory substances present in cells. These bodies (activators or co-enzymes) may be other organic compounds (peroxidases); it appears also that in some cases inorganic salts, especially iron salts, may play this rôle (cf. Warburg[117]). There is some evidence that the combination of hemoglobin with oxygen is of the nature of a peroxid; both hemoglobin and hematin may cause bluing of guaiac, and exhibit other oxidase-like properties.[118] Compounds which form unstable peroxid-like unions with oxygen are regarded by certain investigators as forming the essentially irritable part of the cell; the temporary stabilization of such compounds by any physical or chemical influence would thus be equivalent to an anesthetization.

MATTHEWS' THEORY OF MOLECULAR OXYGEN-PROTOPLASMIC UNION.

This view has recently been supported in the country by Mathews;[119] he regards anesthesia as due to the formation of chemical unions between the anesthetic protoplasm; these unions are due to the residual valences of the anesthetic (i. e. the reserve powers of union left over in many compounds after the ordinary valences are satisfied, as seen in the formation of double salts, and hydrates); the number of residual valences is variable, but tends to be higher in compounds with well marked anesthetic property. Mathews finds a general though not complete parallelism between the number of such valences in a compound and its narcotic power. He proposes the following explanation of anesthesia: "*the irritable substance in protoplasm is a molecular oxygen-protoplasmic union or a peroxid union, unstable and similar to oxy-hemoglobin. By stimulation this unstable molecular union passes by molecular rearrangement into a stable form, oxidation taking place and carbon dioxid being directly or indirectly produced. The anesthetic produces anesthesia by occupying the oxygen-receptors of the cell, thus forming a non-irritable dissociable, anesthetic-protoplasm compound. The various facts of anesthesia are explicable on this theory.*"

Now it is a striking fact that the concentrations of the lipoid-solvent anesthetic required to inhibit oxidations under the influence of enzymes, inorganic catalysts, or dead cells are far higher than for true anesthesia, and are closely similar in their order of magnitude to the cytolytic concentrations. As already mentioned, Vernon found that the concentrations at which the activity of the kidney-oxidase began to be decidedly lowered corresponded closely with those found by Fuhner and Neubauer for hemolysis; i. e. in Vernon's words, "*those which dissolve the lipoid membrane of the corpuscles.*" The concentrations required for anesthesia in tadpoles are from eight to ten times lower. It thus seems doubtful that the anesthetic effects can be referred to a direct inhibitory action on oxidases. The prompt and complete reversibility of anesthesia is also a fact unfavorable to this view. According to Vernon's results tissue-oxidases are rapidly destroyed by those concentrations of lipoid-solvent anesthetics which reduce their activity to half its original value. We find that in those cases where anesthesia is associated with decrease of intracellular oxidations, the inhibitory effect is obtained in relatively low concentrations; while to induce an equal decrease of oxidations in tissue-extracts or in disintegrated tissues or cells the required concentrations are much higher. In other words, destroying the *structure* of the tissue destroys its sensitiveness to the inhibiting action of low concentrations of the anesthetic. This fact seems to indicate that the anesthetics acts on living cells primarily by altering certain organized or structural elements, on the condition of which the normal rate of oxidation and of other metabolic processes depends. Experiments on tissue-extracts indicate that the oxidations in living cells like muscle-cells are far more rapid and

complete than can be effected through the simple agency of the oxidases present (Fletcher and Hopkins, Warburg, Battelli and Stern[120]); the rôle of oxidases in cell-respiration may therefore well be a subsidiary one; and if so, the fact that anesthetics arrest cell-activities in concentrations which are without direct influence on the oxidases may be understood. The essential change in anesthesia would then be a reversible alteration of certain structural elements that control oxidations as well as other cell-processes.

Such a view would regard oxidases as accessory rather than primary factors in cell-oxidations. If this is true, there should be no direct parallelism between decrease of oxidations and anesthesia; and it should be possible in certain cases to secure anesthesia without influencing oxidations. There are in fact numerous instances of complete and typical anesthesia unaccompanied by any essential decrease in the rate of oxidations. The anesthesia of anaërobic animals and yeast-cells has already been cited; this instance, however, may be considered equivocal,—since oxidations are equally essential to metabolism in these organisms, even though molecular oxygen may not take part in the reactions. But many cases are known where the activity of aërobic organisms or tissues may be profoundly inhibited by anesthetics, while the rate of oxidation is unaltered or only slightly decreased. Such lack of parallelism was observed by Rhode and Ogawa for the influence of chloral hydrate on the isolated heart.[121] The case of cell-division in developing eggs is an especially clear one; here the rate of oxidation is relatively slight compared with the active muscle-cells. Warburg found that phenyl urethane, in concentrations of m-2,000, arrests cell division completely in sea-urchin eggs, (Strongylocentrotus), while leaving oxygen-consumption essentially unchanged; in order materially to decrease oxidations (by 40 per cent.) several times the minimal anesthetic concentration was needed (m-500).[122] Similar observations were made by Loeb and Wasteneys[123] on the eggs of another sea-urchin (Arbacia). In order to arrest cleavage by cyanid (which directly inhibits oxidations) a concentration sufficient to lower the rate of oxidation to one-third the normal was needed. The oxidations could be reduced to one-half the normal without arresting cleavage. But in solutions of various anesthetics (chloral, urethane, chloroform, methyl, ethyl, and propyl alcohols) of concentration sufficient to prevent cleavage entirely, the rate of oxidation was found to be only slightly decreased,—on the average by less than 10 per cent. In solutions of urethane during the complete arrest of cleavage, the rate of oxidation was 98 per cent. of the control. When it is considered that oxidations may be decreased by much more than 10 per cent (by means of cyanid, or by lowering the temperature a few degrees) without arresting cleavage, it seems evident that the slight decrease of oxidation observed in these experiments can stand in no causal relation to narcosis. It is an accessory and apparently inessential effect. Closely similar results were found in experiments with young fish embryos (Fundulus), at a stage when the musculature was well-developed so that active contractions could be evoked by external stimulation (as by acidulated sea water). When unstimulated the embryos lie quiet in the egg; the disturbing effects of variations in muscular activity are thus absent. During complete chloroform narcosis there was little or no change in the rate of oxidations; ether and butyl alcohol caused some decrease in oxidations (25 to 30 per cent. at the narcotizing concentrations); but in order to render the animals insensitive by direct inhibitions of oxidation through cyanid it was found necessary to reduce the oxidations to *one-ninth* of their normal rate. In marine medusæ (Gonionemus) paralysis by cyanid required a decrease in oxidations from three to six times greater than that accompanying urethane narcosis.

The insensitivity of many cells and tissues to simple abstraction of oxygen or presence of cyanid is in striking contrast to their sensitivity to anesthetics. Thus nerve trunks only gradually loses irritability and conductivity in an oxygen-free atmosphere, or in cyanid solutions of considerable concentration (Dontas[124]); while the desensitizing effects of anesthesia are rapid and complete. That the two effects are essentially different is further shown by the difference in the rate of recovery, which is much prompter in the case of

anesthesia. Apparently narcosis may decrease the oxidations in resting nerve trunks, as indicated by the output of carbon dioxid; this is seen in the experiments of Tashiro and Adams already cited; but the effect is comparatively slight and probably unconnected with the loss of irritability, since, as just seen, nerves retain irritability in cyanid solutions for a long time. Compare also Winterstein's results, about to be described. Other similar instances are ciliary movement and protoplasmic rotation, both of which are only gradually checked by lack of oxygen or cyanid, but instantly by narcotics. Recently Winterstein[125] has shown that the reflex irritability of the frog's isolated spinal cord may be entirely lost under anesthesia without affecting the general oxidation-rate of the tissue; in fact during alcohol narcosis there was a slight but regular *increase* in oxygen-consumption. The narcotized cord differs from the non-narcotized in one chief respect: in the normal and incompletely narcotized cord stimulation causes increased oxygen-consumption; but during complete narcosis no such effect is seen—the oxygen-consumption is the same as in the resting non-narcotized cord. Oxygen is, however, essential for the normal irritability of the cord; complete recovery from narcosis requires not only removal of the anesthetic but also the presence of free oxygen. There may however be *partial* recovery even in the absence of oxygen. These facts illustrate how important oxygen is to the normal activity of the nerve-cell; but they also show that, given a supply of free oxygen, the consumption in the normal resting cord may be the same as in the narcotized cord. If narcosis were simply asphyxia, such a result would be inexplicable. A further fact inconsistent with the *asphyxia hypothesis* of narcosis is that after a narcosis lasting for days (9 days in one of Winterstein's experiments with urethane) reflex irritability returns promptly on the removal of the anesthetic. There is no evidence that nerve-cells can resist lack of oxygen for any such time. There is, however, ample evidence from other sides that during narcosis the normal resting oxidations of tissues continue uninterruptedly. Winterstein also finds that the oxidative removal of acid products of asphyxia takes place equally readily in normal and in narcotized nerve-cells. The central nervous system of the frog, which normally exhibits an alkaline reaction to litmus, becomes acid during asphyxia if oxygen is then restored the alkaline reaction returns; but narcosis was found to have no influence on this effect; clearly therefore, narcosis does not interfere with these oxidations.[126]

Such observations should be correlated with those of Vernon, Warburg, and Battelli and Stern cited above, *indicating that tissue-oxidations are directly influenced only by relatively high concentrations of anesthetics.* Taken in conjunction with the other instances just cited, of anesthesia with essentially unaltered rate of oxidation, they indicate that a *direct suppression of intracellular oxidations (or asphyxia) is probably not the essential basis of anesthesia.* Apparently the latter condition does not depend on any alteration of purely chemical conditions, but on some influence exercised by the anesthetic agency on the structural or organized or *living* substratum in which the chemical processes take place and by which their character and rate are controlled. The evidence of this will now be considered.

DEGREE OF ORGANIZATION AND SUSCEPTIBILITY TO NARCOSIS.

There appears to be a general relation between degree of organization and susceptibility to narcosis. Plants and lower organisms require higher concentrations of anesthetic than higher animals (Overton); in vertebrates the cells most susceptible to narcosis are those of the higher brain-centers. Such cells are distinguished by high irritability and rapid variations in their activity,—peculiarities which are undoubtedly a function of their special structure. It is true that if organization is destroyed many of the chemical processes of protoplasm (oxidations and fermentations) may still continue (antolysis) and may then be slowed by anesthetics; but, as already shown, much higher concentrations are required to produce this effect than to anesthetize the intact living cells. Such facts indicate that when anesthetics influence oxidative and other metabolic processes within the cell, they do so not directly, but through

their influence upon some specially sensitive intermediary, which is a part of the organized structure of the cell and itself controls the rate of the intracellular chemical processes. It is this intermediary which is directly influenced by the anesthetic. Its part may be compared to that of a sensitive *starter* or relay in a complex mechanical or electrical system.

Various general considerations support this view. When an irritable element, e. g. a muscle-cell, is stimulated by a mechanical impact, it is difficult to suppose that the primary effect of this impact is to hasten oxidative processes. It is true that an increase in oxidation does follow, but this effect represents a later stage in the complex sequence of interdependent processes constituting the response to stimulation (and of which the contraction is the most evident). If the muscle is previously treated for a short time with an anesthetic, or if the magnesium or calcium-content of the medium is sufficiently increased, contraction no longer results. The entire sequence of processes normally following stimulation is prevented. It seems more probable that the *primary* event in the physiological sequence is the one directly interfered with; if this is prevented so also are the others. It further seems clear that in an irritable cell this primary or determinative change must be a *surface-change;* obviously that part of the irritable element which is directly in contact with the medium is the one first affected by the stimulus; and there is ample evidence that the direct action of many stimuli is confined to this surface-layer. Obviously the activity of the whole cell is affected; this, however, must be by means of some influence transmitted from the surface throughout the cell-interior. The nature of this influence forms the chief problem of the physiology of stimulation.

The fact that a surface-effect is sufficient to set in motion the whole complex apparatus of response in the cell-interior is a cardinal one in any theory of anesthesia. Unmistakable evidence that this is the case is seen in the delicacy of the response which sensitive organisms like protozoa show to the contact-stimuli of food-particles or prey; also in the prompt response of many living cells to the presence of substances which are known from experiments on permeability not to penetrate the plasma-membranes. In general these membranes in their normal state are impermeable to the neutral salts of the alkali and alkali-earth metals, as Overton has shown; yet variations in the proportions of such salts in the tissue media profoundly influence the activity and irritability of living cells. Increase in the magnesium or calcium salts of the medium may cause typical anesthesia in muscle and nerve cells. Warburg and Harvey[127] have shown that cell-division in sea-urchin eggs may be arrested by weak solutions of sodium hydrate without the alkali penetrating the cell. A. J. Clark has made similar observations for heart muscle-cells, and Harvey for the contractile cells of medusæ and for protoplasmic rotation in plant-cells.[128] Irritability and automatic activity may thus be abolished by substances to which the cell-surface is impermeable. The general facts of electrical stimulation also indicate that alteration in the electrical condition of the cell-surface is the primary event in stimulation. The investigations of Nernst and his successors on the theory of electrical stimulation show that the electrical current stimulates by changing the relative concentrations of ions on the opposite faces of the semi-permeable membranes enclosing the irritable elements,—*i, e.*, by altering the electrical polarization of the surface-film or plasma-membrane of the cell. A characteristic electrical variation, the action current— which is best explained as the result of alterations in the electro-motor properties of the cell-surface,—accompanies all forms of stimulation; and this electro-motor variation is prevented by anesthetics. It may be held therefore with a high degree of probability that the primary event in stimulation is a *surface-process*, consisting in some physico-chemical alteration of the modified protoplasmic surface-film (plasma-membrane) which delimits irritable cells.[129]

THE PHYSICO-CHEMICAL ALTERATION OF PLASMA MEMBRANE AS A BASIS OF ANESTHESIA.

Lately many investigators have concurred in this view that alterations in the physico-chemical properties of the plasma-membrane form the essential basis of anesthesia. Whatever condition alters this structure so as to make it less capable of undergoing the changes

of permeability and of electrical polarization which normally accompany stimulation—and apparently other forms of cell-activity—has an inhibiting or paralyzing effect on the cell. This general view has been reached as the outcome of a large number and variety of investigations. Overton in 1904 pointed out that the paralyzing action of potassium salts on voluntary muscle must be referred to their action on the membrane, since plasmolytic experiments indicate that such salts do not penetrate into the cell-interior.[130] The view that the physiological action of neutral salts is due primarily to their influence on the plasma-membrane was later strongly supported by Höber,[131] on the basis of experiments on the influence of neutral salts on the demarcation-current potential of muscle. This may be influenced in the direction of either increase or decrease by treatment with isotonic solutions of sodium and other salts. Salt-solutions, like those of potassium salts, which decrease this potential—*i. e.* produce local negative variation—apparently do so by altering the colloids of the plasma-membrane and so increasing its permeability; in general such increased permeability to ions involves decrease in the electrical polarization of the membrane (or negative variation); increased polarization means an alteration of the membrane in the reverse direction, *i. e.* of decreased permeability. These changes of polarization and permeability depends on the altered condition of the colloids forming the membrane. The colloidal system of the membrane acquires in the presence of certain salts a less dense consistency (*Auflockerung*), associated with increased permeability; and a denser consistency (*Verdichtung*) in the presence of others (*e. g.* sodium iodide, etc.) The microscopic appearances observed in nerve-fibres treated with pure solutions of sodium and potassium salts support this conception.[132] Changes in the electrical conditions of the cell are thus indices of changes in the colloids forming the plasma-membrane, and especially in the lipoids. Now, since the stimulation-process is always accompanied by electrical variations, it seems probable that this process is dependent on changes in the colloids of the plasma-membrane, involving changes of permeability; correspondingly, artificial alterations in the condition of these colloids should modify the irritability of the cell.[133] In an important paper published in 1907, entitled "Contributions to the Physical Chemistry of Stimulation and Narcosis,"[134] Höber applies this general conception to the problem of narcosis, essentially as follows: *Stimulation is associated with an alteration in the condition of the colloids of the plasma-membrane, involving a general increase of permeability; narcotics are those agents which prevent this alteration in the condition of the proto-plasmic colloids and hence prevent stimulation. The colloids chiefly concerned are the lipoids; narcosis depends on the collection of lipoid-soluble substances in the lecithin of the plasma-membrane to a certain critical concentration, and on a prevention, by means of these substances, of the colloid-process normally concerned in stimulation.* Höber showed that various anesthetics (ethyl and phenyl urethane, chloral hydrate, chloroform, hypnon) do in fact check the action of rubidium and potassium salts in causing negative variation in frogs' muscle. They also prevent the effect of potassium sulphate in causing structural changes (*Auflockerung*) in nerve. The anesthetic thus antagonizes the salt-action, just as it is known to antagonize the stimulating action. Similar effects may be produced by alkali earth salts, especially of calcium. According, therefore, to Höber's hypothesis, *the physico-chemical basis of these antagonisms, and hence of anesthetic action in general, is an alteration of the colloids, especially the lipoids, of the plasma-membrane, and a consequent change in the properties of this structure.* The temporary increase of permeability, which, according to Bernstein's theory of the bioelectric variations, forms an essential part of the stimulation-process, is thus rendered difficult or impossible.

Very clear and concrete indication that the stimulation of muscle is in fact associated with a temporary increase in the permeability of the plasma-membrane, and that anesthetics act by preventing this increase, was afforded by my own experiments on the larvæ of the marine annelid Arenicola, carried out at Woods Hole in 1908.[135] This larva is a free-swimming trochophore one-third of a millimeter long, possessing a well developed musculature and swimming by cilia, and is peculiar in hav-

ing its body-cells permeated by a brown water-soluble pigment. This pigment normally remains within the cells; but under conditions of increased permeability, as on death or under the influence of cytolytic substances, it diffuses readily into the sea-water and imparts a yellow tinge to the latter. It serves therefore as a convenient indicator of increase of permeability. If larvæ are brought suddenly from sea water into a pure isotonic solution of a sodium salt (*c. g.* 0.6m NaCl), a strong muscular contraction at once results, accompanied by a well-marked loss of pigment; at the same time the cilia cease movement, soon undergoing breakdown, and other toxic effects follow. If, instead of a *pure* solution of NaCl, a solution containing $CaCl_2$ or $MgCl_2$ is used, both changes are simultaneously prevented; neither contraction nor loss of pigment is shown; the cilia remain active, and normal swimming movements continue for a time; the general toxic action of the pure salt-solution is also prevented. Thus the calcium prevents at the same time both the stimulating and the permeability-increasing action of the sodium salt. It also greatly diminishes the injurious action of the latter; exerting an anti-toxic action. Pure solutions of KCl also cause strong muscular contractions accompanied by loss of pigment; and the effect is similarly checked by the addition of MgI_2. In mixtures of KCl and $MgCl_2$ both effects vary with the Mg-content of the solution in a closely parallel manner; solutions with relatively high Mg-content cause slight stimulation and slight loss of pigment, while in those of relatively high K-content both effects are well marked.

Entirely different effects from those of pure solutions of potassium and sodium salts are produced by pure solutions of magnesium salts. These exert typical anesthetic action on Arenicola larvæ, as on other marine animals. When brought suddenly into pure isotonic $MgCl_2$ solution the larvæ show no contraction or loss of pigment; all muscular contraction immediately ceases, the body remains rigid and extended; the cilia are more resistant and remain active, and slow undirected swimming movements continue. On return to sea water muscular movement and other normal activities are at once restored. If larvæ are brought into isotonic $MgCl_2$ solution for a few minutes, and are then transferred into pure NaCl solution, the characteristic effects following transfer to the solution from sea water—stimulation and loss of pigment—are no longer seen; the organisms remain motionless and without apparent change. If then returned to sea water they show prompt revival. Apparently the treatment with $MgCl_2$ renders the plasma-membrane more resistant than normally to the permeability-increasing action of the pure NaCl solution, and at the same time the muscle-cells become refractory to stimulation. The following was the conclusion drawn at the time from these facts: *$MgCl_2$ and similarly acting solutions appear to decrease the permeability of the tissues and so prevent the ionic transfer on which stimulation depends. The general action of anesthetics consists in decreasing the normal permeability; stimulating agencies on the other hand have the reverse effect.*"[136] Later experiments with a variety of lipoid-solvent anesthetics—alcohols, esters, ether, hydrocarons—gave essentially similar results;[137] solutions of anesthetics in pure NaCl solution, in every case where they prevented the stimulating action of the solution, also prevented the permeability-increasing action, as indicated by loss of pigment; when they did not prevent this effect they did not prevent stimulation. A general parallelism between prevention of permeability-increasing action and prevention of stimulation was thus shown. Anesthetics were also found to prevent other effects depending on increase of permeability, such as the toxic effects of pure solutions of Na and K salts on sea-urchin and starfish eggs as well as on Arenicola larvæ,[138] and also the activation of unfertilized sea-urchin eggs by pure salt-solutions (KCNS, Na I).[139] *In general the anesthetics appear to exert a stabilizing action on the plasma-membrane, rendering it more resistant than normally to influences that tend to increase its permeability. To this stabilizing action both the inhibitory or anti-stimulating (anesthetic) and the protective (anti-toxic) actions of both salts and lipoid-solvent anesthetics are due.*

Recently a large body of evidence has accumulated from various sides indicating that anesthetics either decrease the permeability normal to the resting cell, or render the plas-

ma-membrane more resistance than normally to increase of permeability. Thus, according to Lepeschkin,[140] the entrance of dyes into plant cells (Spirogyra) is checked in the presence of low concentrations of ether and chloroform, and according to Szucs,[141] also by neutral salts. I have made similar observations on Arenicola larvæ.[142] These effects indicate a decrease in the general permeability of the plasma-membrane to diffusing substances. This change is apparently associated with a characteristic change in the density or physical consistency of the membrane, rendering it more than normally resistant to disintegrative or toxic agencies in general. This explains why anesthetics as well as neutral salts protect the cilia, pigment cells and musculature of Arenicola larvæ against the injurious action of pure Na-salt solutions; the same is true of sea-urchin and starfish eggs. Similar observations are recorded in the literature. Arrhenius and Bubanovic[143] find that blood-corpuscles may be protected by anesthetics against cytolysis in hypotonic solutions; and Traube has made similar observations for solutions of cytolytic substances (hemoglobin).[144] The increase in permeability caused by pure solutions of Na-salts in fish eggs is also decreased by alcohol and ether, according to McClendon;[145] and Loeb has described similar effects of alcohol on Fundulus eggs.[146]

REDUCED ELECTRICAL CONDUCTIVITY DURING NARCOSIS DUE TO DECREASED PLASMA-MEMBRANE PERMEABILITY.

The most conclusive evidence of a decrease in permeability during narcosis is, however, derived from experiments on the electrical conductivity of narcotized cells; this appears to be decreased during narcosis (McClendon, Osterhout, Höber and Joel). McClendon in 1910 found the conductivity of sea-urchin eggs to be decreased by chloroform, but did not investigate the phenomon in detail. More extensive experiments have since been carried out on plant cells by Osterhout,[147] who has succeeded in showing clearly that in the presence of moderate concentrations of anesthetics like ether the cells of the marine alga Laminaria undergo increase in electrical resistance, indicating decreased permeability to ions; on removing the anesthetic the original conductivity returns. If too high concentrations of anesthetic were used the result was quite different; conductivity underwent marked increase and the effects were irreversible; the tissue had in fact undergone an injurious or cytolytic alteration. Evidently the change corresponding to anesthesia is the reversible change of *decreased* conductivity, indicating decreased permeability. Similar observations on blood-corpuscles have recently been made by Joel under Höber's direction.[148]

Taken in its entirety the foregoing evidence indicates that under the influence of a narcotizing agent the plasma-membrane undergoes an increase in its general stability or resistance to alterations; stimulation is prevented because this effect requires ready and rapid variations of permeability, and of these the stabilized membrane is no longer capable. Associated with this general stabilization is a decrease in the permeability in diffusing substances; the cell is more completely shut off from the disturbing effects of environmental changes. There is a possibility that the permeability to gases like carbon dioxid and oxygen is also decreased, but this remains uncertain at present.

It is important to note that changes in the resistance of plasma-membranes, probably essentially similar to those underlying anesthesia, may in fact occur under completely normal conditions, as I have recently found in experiments on dividing sea-urchin eggs. It had been shown earlier by Lyon,[149] Spaulding,[150] and Mathews[151] that during the normal cycle of cell-division these cells are much more susceptible to poisons (cyanid, acids, ether, and K-salts) at the time when the cleavage-furrow is forming, than in the period preceding or following cleavage; during cleavage there is also an increased output of CO_2.[152] A rythm of susceptibility to poisons and CO_2-production is thus associated with the rhythm of cleavage. This condition suggested the possibility that the essential underlying condition of this rhythm might be a rhythmical change in the properties of the plasma-membrane; and in a series of experiments with dilute sea water it was found that the eggs do in fact undergo cytolysis in hypotonic media

far more readily at the time when the furrow is forming than during the intervals between cleavage. In other words, the membrane is relatively sensitive to osmotic disruption during cleavage, and relatively resistant during the intervals between cleavage, *i. e.*, at the resting times when the cell is relatively highly resistant to the action of poisons. This normal state of relatively high stability may be compared to the condition which is imparted to the membranes of irritable cells by anesthetics. Increased resistance to hypotonic solutions in the presence of anesthetics has been observed by Arrhenius and Bubanovic in blood-corpuscles, as already cited.

THE MECHANISM OF THE PHYSICO-CHEMICAL BASIS OF ANESTHESIA.

How does the anesthetic produce this alteration in the properties of the membrane? Attempts to find parallels between the effects of anesthetics on living cells and on colloidal suspensions of lipoids have not given entirely consistent results. Höber and Gordon[153] found that lecithin suspensions containing ether, chloroform, chloral, or amyl alcohol were less readily precipitated by calcium and barium salts than the control suspensions, *i. e.*, were protected against precipitation or stabilized by the anesthetic; and they refer to this phenomenon as "*narcotization of the plasma-membrane colloid lecithin.*" Koch and McLean,[154] on the other hand, find that no such effect is general with anesthetics; they find chloral and ether indifferent, while chloroform protects lecithin against precipitation by $CaCl_2$; alcohol and paraldehyde on the other hand further precipitation. These discrepancies are probably due to differences of concentration. Recent experiments of my own with a large number of anesthetics have shown that with the great majority of such compounds lecithin emulsions may be protected to a greater or less degree against the precipitating action of $CaCl_2$ and HCl; *i. e.*, a concentration of electrolyte just sufficient to cause precipitation in the absence of the anesthetic fails to do so or does so incompletely in its presence. The concentrations required to produce this stabilization are, however, much higher than the anesthetizing concentrations, and the various compounds vary greatly in effectiveness. The usual increase of action with increasing molecular weight in members of homologous series (alcohol, esters) was seen. But with certain compounds little or no protection was found; while a few (ethyl and methyl alcohols and in part isopropyl alcohol, acetonitrile and in part paraldehyde) definitely furthered precipitation. The compounds which distinctly prevented precipitation included higher alcohols (n-propyl, n-butyl, i-amyl, capryl,) esters (ethyl nitrate, propionate, butyrate; methyl, ethyl and phenyl urethanes), hydrocarbons (chloroform, carbon tetrachlorid, nitromethane, benzol, toluol, xylol), ethyl ether, chloral hydrate, chloretone, chloralose, acetanilid, phenyl urea. In general, therefore, it would appear that lipoid-solvent anesthetics may exert a stabilizing influence against precipitation by electrolytes, but this influence is not always present. It may depend upon altered electrical polarization of the colloidal particles, or possibly upon increase of viscisity; but it is doubtful if in itself it forms a factor of any importance in true anesthesia. The effective concentrations are too high and the effect is too variable.

A probably more significant physical change caused by lipoid-solvent anesthetics is an increase in the viscosity of lecithin suspensions. Handowsky and Wagner[155] observed such an increase of viscosity in the presence of alcohol; and A. Thomas, working in my laboratory, has confirmed and extended these observations. Thomas observed that in the case of ether the increase of viscosity in concentrated emulsions of lecithin might go so far as to cause true gelation. I have found that this effect is very general; it is well shown in lecithin emulsions of 10 to 12 per cent. concentration; these are highly viscous, but still fluid in consistency; on the addition of many anesthetics the consistency changes to that of a soft more or less coherent and elastic gel, in some cases of sufficient firmness to permit the inversion of the test-tube without spilling. Well marked gelation was observed with the following compounds:—alcohols, (n-propyl, i-propyl, n-butyl, i-amyl, capryl), esters (ethyl formate, acetate, propionate, butyrate, nitrate), ethyl ether, ethyl chlorid, ethyl bromid, chloroform, carbon tetrachlorid, benzol, toluol, xylol,

chloretone, chloral hydrate, chloralose, paraldehyde. On the other hand certain very efficient narcotics had no such effect, e. g. methyl, ethyl and phenyl urethanes, ethyl alcohol, nitromethane, and acetonitrile. Gelation, however, is to be regarded simply as an end-effect of increase in viscosity; the latter change is the essential, and this is perhaps the most general and significant of the purely physical changes produced by lipoid-solvent anesthetics in colloidal suspensions of lipoids. Such a change will have a generally retarding influence on physical and chemical processes taking place in such a system; it will decrease diffusion-rates, and hence reaction-velocities depending on such rates; in general more energy, mechanical or other) is required to produce any kind of change in a highly viscous system. A general hindrance to diffusion would express itself in a decrease of permeability and of electrical conductivity. The influence of changing viscosity on the electrical conductivity of lipoid suspensions remains to be studied. Recently Loewe[156] has investigated the influence of various anesthetics on the electrical resistance of solid artificial membranes impregnated with lipoids; and he has found that in some cases they cause decided decrease of conductivity,—a change to which he refers as "*narcosis of the membrane.*" These results recall those of Osterhout on living plasma-membranes, but whether the anesthetic effect in living cells is so direct as Loewe's experiments would indicate is perhaps doubtful.

On the whole it appears highly probable that lipoid-solvent anesthetics cause their effects through some purely *physical* change in the cell-system—particularly in the plasma-membrane. Their chemical inactivity as a class indicates this. Processes like solution and adsorption rather than chemical combination probably determine their action in most cases. It is, however, best not to be too dogmatic on this point, since the distinctions between solution, chemical combination, and adsorption are probably not absolute. There is always the possibility that in certain cases the anesthetic may form some chemical combination which interferes with chemical or other changes necessary to stimulation; the inactivation of hemoglobin by carbon monoxid may serve as an illustration of how this is possible. Höber[157] has recently suggested that in true reversible narcosis the direct effect of the anesthetic is limited to a surface-action or adsorption affecting all of the colloids of the membrane; in higher than the narcotizing concentrations the solvent action of the anesthetic upon the lipoids of the membrane assumes importance and leads to disruptive and hence irreversible effects. This view attributes the destructive action of anesthetics in high concentrations to a process different from that underlying true anesthesia. Meyer's experiments on the effects of temperature already cited indicate, however, that solution of the anesthetic in the lipoids is an essential factor in the total physiological effect. It is conceivable that a slight solution of this kind, combined with a general increase in the viscosity of the protoplasmic surface-layer, may increase the stability of the membrane; while a more pronounced solution may lead to direct solvent or other structure-altering effects which destroy its semi-permeability and so cause cytolysis.

It must not be forgotten, however, that lipoid-solvents form only one class of anesthetics. Apparently all substances or conditions which stabilize the membrane in a reversible manner may exert anesthetic action. Anesthesia due to neutral salts, cold or the electric current may be understood from this point of view; salts or low temperature may stabilize the membrane by causing gelation or other direct changes of aggregation in the colloids; the electric current by altering its state of electrical polarization. Some years ago I expressed this general view as follows: "*anesthetic action is due primarily to a modification of the plasma-membrane of the cells or irritable elements, of such a kind as to render these membranes more resistant towards agencies which under the usual conditions rapidly increase their permeability; cytolysis and stimulation, both of which depend on such increase of permeability, are hence checked or prevented. Decrease in the readiness with which the permeability is increased thus involves for an irritable tissue decreased irritability; this effect is produced by various salts, e. g. of magnesium, and by ether and other lipoid-solvent anesthetics in certain, not too high, concen-*

trations. . . . . It seems clear that for irritable tissues the state of the lipoids in the plasma-membrane largely determines the readiness with which changes of permeability—and of the dependent electrical polarization—are induced by external agencies. Slight permeation of the lipoids with a lipoid-solvent apparently often facilities such changes, and hence increases irritability; the presence of more lipoid-solvent renders a change of permeability difficult, hence the protective or anesthetic action; while concentrated solutions of lipoid-solvents disrupt the membrane and produce cytolytic or irreversible alterations in the cells; hence such substances in higher concentrations are markedly toxic."[158]

The question of just how this stabilizing influence is exerted is the critical one. An irritable element like a nerve-fibre or muscle-cell responds to a slight local electrical stimulation or mechanical impact; this response is apparently associated with a rapid and reversible increase of membrane-permeability; to this latter change the electrical variation is apparently due. It is the membrane-change, with the associated variation of electrical polarization, which appears to be the primary physiological event in stimulation; it spreads rapidly over the whole membrane, and the other consequences of stimulation (contraction, increased oxidation, etc.) follow upon this surface-change. The question thus involves the whole problem of the physiology of stimulation. This is not the place for a detailed discussion of the various questions involved in this central problem. It is evident, however, that the whole process of stimulation depends on the local initiation of the excitation-state, and on the rapid conduction of this state from the point of stimulation so as to effect the entire element.[159] All of these processes depend on the physical and chemical condition of the membrane; hence altering this condition alters the whole stimulation-process.

According to this conception the sensitivity of the membrane to changes of electrical polarization is its most characteristic peculiarity.[160] The basis of this sensitivity remains to be determined. It would appear that the peculiar properties of the membrane depend upon its being a *living* structure, the seat of a specific metabolism. That the characteristic semi-permeability depends on this latter peculiarity is seen in the fact that the death-process, however induced, is always associated with a marked increase in the general permeability and electrical conductivity of cells. In other words, the normal semi-permeable condition—involving, as it must, a certain constancy in the composition and physical state of the surface-film—is maintained only so long as the cell remains alive. This fact shows that semi-permeability, and the electrical polarization which is associated with this, are not simply static properties of the plasma-membrane, but are functions of a specific metabolic activity—including probably oxidations in most cases—which maintains constant the physico-chemical characteristics of the surface-layer of protoplasm. In the irritable element this metabolism appears to be altered in a definite manner by changes in the electrical polarization of the membrane; and along with these chemical alterations go alterations of permeability and, secondarily, of electrical polarization. These latter involve the production of local electrical circuits which traverse and hence stimulate the adjoining inactive portions of the irritable element; in this manner the state of excitation *spreads*, and the whole element is stimulated.[161] But this is the case provided only that the membrane retains its normal sensitivity to changes of electrical polarization; if it has previously been rendered resistant by an anesthetic, no such effect follows; the element as a whole then shows itself irresponsive to stimulation.

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tion varies directly with its solubility in the material composing the partition. Flusin's experiments with rubber membranes are a good instance of this. The diffusion of substances through the surface-films bounding the cells implies a passage either through or between the membrane-constituents; and in the case of the living cell, solution of lipoid-soluble substances in the lipoids of the membrane is probably the main factor in their entrance, although this entrance may be favored by adsorption due to surface-activity.

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BLOOD CHANGES UNDER ANESTHESIA AND ANALGESIA • REVIEW OF THE BIBLIOGRAPHY • RECENT RESEARCHES OF MENDENHALL ON THE COAGULATION TIME OF THE BLOOD AS AFFECTED BY ANESTHETICS • MENTEN AND CRILE ON THE H-ION CONTENT AS AFFECTED BY EMOTIONS, SHOCK AND ANESTHESIA • PERSONAL EXPERIMENTS OF THE AUTHOR AND E. Q. ST. JOHN ON BLOOD CHANGES UNDER NITROUS OXID-OXYGEN IN MAN AND RATS, WITH DETAILED TABULATION OF RESULTS.

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IN ORDER TO OBTAIN a comprehensive appreciation of the blood changes under anesthesia it seems advisable to review the literature of this subject in chronological order, for each author and investigator has drawn something of interest and importance from the clinical and experimental results that have preceded his own research work.

The three principal anesthetic agents, ether, chloroform and nitrous oxid were developed almost synchronously and any investigation of the one was usually influenced by comparison with the other two.

It is unnecessary at this time to dwell upon the many points in dispute that have arisen over the credit due to those pioneers who were foremost in the discovery and use of anesthetics for the alleviation of pain. In this paper, however, every effort will be made to accord those investigators of blood changes under anesthesia, the credit due them for their original researches.

The physiological basis and histo-pathology of anesthesia have not kept pace with its clinical development. Often the data colated from long series of operative cases have been complicated by serious pathological conditions, which have materially influenced the findings, whereas the study of this subject should be made on healthy individuals or animals free from conflicting medication or surgical shock, to arrive at normal results. Fortunately clinical results have frequently paralled those of experimental researches on animals, and these incidences have helped to establish some fundamental facts as a working basis for future researches.

In making examinations for blood changes under anesthesia, the following questions must be constantly borne in mind: (1) Is the hemoglobin increased or decreased? (2) Does anesthesia precipitate a polycythemia or oligocythemia? (3) What changes occur in the color index? (4) Is hemolysis marked? (5) Is there leukopenia or leucocytosis? (6) What cellular alterations occur in the polymorphonuclear, small and large lympocytes, transitional forms, eosinophiles or basophiles? (7) Does segmentation of the polynuclear neutrophiles occur, or (8) does the number of blood platlets change? (9) Is there an increase of the blood's acidity as indicated by the H-ion content? (10) What is shown by the spectrum analysis? and (11) which of the two theories of anesthesia as produced by nitrous oxid is the more tenable, that of deoxygenation and asphyxiation or a specific physico-chemical action on the brain?

CHLOROFORM RESEARCHES OF SANSOM.

Early in the evolution of anesthesia, Sansom reported on his experimental work on blood changes under chloroform to the Royal Society of Medicine, London.[1] Most of these experiments were carried out by putting blood in test tubes with the anesthetic agent and noting the physical and chemical changes taking place under these conditions, and the conclusions drawn from these observations were

that: Chloroform exerts a caustic action on the protenous cell wall of the blood corpuscles; this action being manifested by, (1) corrugation of the cell walls and alterations of shape; (2) coherence of corpuscles and (3) instant stasis of the circulating blood when liquid chloroform permeates the living walls of the blood vessels.

The circulation in the web of a frog's foot, as seen under the microscope, is modified by the vapor of chloroform: (1) The velocity of the circulation is primarily increased, with (2) dilation of the arteries and capillaries; (3) then the velocity of the circulation is decreased; (4) alterations of the cell walls of the corpuscles and coherence occur, after which (5) the capillary circulation is interrupted by those cohering masses, eventuating in (6) stasis of the blood.

The enlarged capacity of the arterial system and the decrease of the circulation account for the anemia of the brain observed during chloroform narcosis. Sansom concluded that: (1) *Chloroform narcosis is due to the imperfect stimulus of the vital function of maloxygenated blood; (2) that this maloxygenation is due to direct influence of chloroform vapor on the blood, especially on the blood corpuscles; and that (3) the vapor acts caustically on the cell walls of the blood corpuscles.*

THE INVESTIGATIONS OF GARRETT, OLIVER AND HERMAN.

In 1863, Garrett and Oliver,[2] studied the effects of anesthetic agents, especially chloroform and their conclusions were that: they deoxidize the blood and tissues and induce malnutrition and the formation of quantities of waste products, the elimination of which induces a severe and possibly dangerous or even fatal strain upon the excretory glands.

Coincident with the test tube experiments conducted by Sansom and the animal experiments of Garrett and Oliver, is the report of Herman,[3] in 1864, on nitrous oxid gas. His conclusions are, it would appear, that while laughing gas is very readily absorbed by the blood, it neither enters into combination with nor produces changes in, nor suffers changes from the action of the blood. On the contrary, it merely is physically absorbed and the blood will take up rather less of it than it will of water; that is to say, 100 volumes of blood will, at body temperature, absorb less than 60 volumes of laughing gas. Blood saturated with laughing gas shows no signs of changes. The spectrum is the same; the blood corpuscles are unaltered and the oxygen is not driven out.

HARLEY'S OBSERVATIONS ON THE EFFECTS OF C. E. MIXTURES.

In a paper read before the Royal Medical and Chirurgical Society in 1864, Harley,[4] described the effects produced by the mixtures of chloroform and ether with the blood, and this report makes the following comparisons: (1) Chloroform diminishes the power of the constituents of the blood to unite with oxygen and give off carbonic acid; whereas sulphuric ether neither diminishes the absorption of oxygen nor the exhalation of carbon dioxid; (2) Chloroform has not nearly so powerful an effect in destroying the red blood corpuscles as ether; the latter rapidly dissolves the cell walls and sets the contents free; (3) Ether has a much more energetic effect in causing the constituents of the blood to assume a crystalline form, and (4) Ether prevents the blood from assuming an arterial tint when agitated with air, while chloroform does not prevent the occurrence of this normal change in color.

THE EXPERIMENTAL RESEARCHES OF M'QUILLAN.

A very exhaustive research was carried on in 1868-1869 by Dr. John H. M'Quillan,[5] physician and dentist, and Professor of Physiology in the Philadelphia Dental College. He illuminated his paper with a number of drawings and wood cuts showing that in accordance with his interpretation of blood smears, made during anesthesia, there was very little or no change in the shape of the cells, and he remarks in conclusion: "It seems to me that the experiments recorded demonstrate that we are not warranted in denying that these (anesthetic) agents act directly upon the nerve centers. All the phenomena attendant upon their administration, the gradual exaltation of the

cerebral functions followed by the progressive impairment and temporary suspension of the special senses, the loss of coordination on the part of the cerebellum, and when the agent is pushed too far, the arrest of respiration and circulation through the decided impression made upon the medulla oblongata, seem to favor the hypothesis, in contradistinction to the theory, that anesthesia is due to suspension of oxygenation.

"In connection with this I cannot refrain from saying, when taking into consideration the readiness with which fluids absorb gases. that undue prominence apparently has been given by physiologists to the blood corpuscles as the carriers of oxygen to the tissues and carbonic acid to the lungs, for it is reasonable to infer that the liquor sanguinis is actively engaged in this operation.

"After the most careful examination under the microscope I have been unable to observe that these modifications in the form of the corpuscles in the venous and arterial blood, changing from biconvex to biconcave discs, and attributable to the absorption of the gases, of which so much has been said in the books. That anesthetics, when acting directly upon the nerve centers, may interfere with oxygenation of the nervous mass, is possible, but it is to be viewed rather as an effect than as a cause of narcosis. Again, even admitting that such agents as chloroform and ether, by interfering with natural respiration and the oxygenation of the nervous mass, might possibly produce their result in that way, it is difficult to understand how this could apply to such an agent as nitrous oxid, which contains an excess of oxygen over atmospheric air."

Dr. M'Quillan had a very clear vision of things to be studied and solved in anesthesia as related to morphology, physiology and chemistry of the blood changes and it must be regretted that his life was not prolonged to carry out his inspirations to a successful conclusion.

BUXTON AND THE PHYSIOLOGY OF NITROUS OXID.

A review of the bibliography of blood changes under anesthesia would not be complete without some quotations from the extensive work of D. W. Buxton[6] on the physiology of nitrous oxid. Buxton holds in part:

"So thin is the wall of the acinic air cells that the lungs may be considered as consisting of aeriform matter, separated from the liquid matter by an exceedingly tenuous membrane, which is capable of the active interchange of gases from the aeriform matter to the liquid matter and vice versa. Whatever aeriform body is inhaled into the lungs, provided it does not impede the mechanical acts of respiration, can diffuse into the blood, while the gases in the blood can diffuse out into the free air space of the lungs. Gaseous bodies, we know, exist in at least two conditions in the blood, (1) in mere solution, and (2) in combination with the albumenoids found in the corpuscles and serum. The essential conditions of life for the organisms are in proportion as the bodily tissues are split up for the production of movement, or force, heat, electricity and so on, so should the blood obtain organic material from the alimentary tract and oxygen wherewith to build it into tissues; and secondarily, that the blood shall be also deputed of organic and saline refuse and of aeriform impurities through mechanism supplied by the lungs. This, I need hardly remind you, consists in the diffusion of carbonic acid gas and other obnoxious materials from the blood into the residual air and into the air spaces and the diffusion into the blood of the oxygen from the residual air. So long as the oxygen tension is higher and the carbonic acid tension is lower in the residual air, so long will the interchange between blood gases take place. When, however, other aeriform bodies than air find their way into the air spaces of the lungs, other conditions are imposed upon the organism. Let us consider these. If the gas be respirable and actually enters the lung space it will obey the laws of the diffusion and in the course of time displaces the residual air. Then being brought into contact with the blood, it will either simply allow of diffusion out of the blood gases; and provided its tension in the lungs is above that of the blood, diffuse into the circulation and so reach the tissues, there to be rejected or built into their substance according as it is available for their metabolism or not, and

if it is able to link itself into chemical union with some constituent of the blood, it will travel so combined to the tissues, where it will more or less profoundly influence their behavior according to its own vital peculiarities.

"Let us consider to what class nitrous oxid belongs and what is the role it plays in the blood. Priestly found that nitrous oxid was readily absorbed by water in the proportion of one-half its bulk. When carbonic acid gas is present in the water no absorption of nitrous oxid takes place, but according to careful experiments of Davy, when water saturated with nitrous oxid is brought into contact with carbonic acid the latter ousts the nitrous oxid, becoming absorbed while nitrous oxid is obliterated. According to the same authority nitrous oxid will displace oxygen and air from water. When we remember that blood consists of 78 per cent. water, we see that these researches have a very important bearing. Neutral saline solutions, further, possess very feeble attractions for nitrous oxid. None of the older observers investigated the behavior of nitrous oxid toward water in which albumenous material was present, and my investigations in this direction are not, I think, sufficiently definite for me to venture upon ex-cathedra utterances; but is seems possible that albumenous solutions of various strengths are possessed of powers of absorbing nitrous oxid other than those inherent in pure water.

"The presence of nitrous oxid in the air space of the lungs is of importance in the following relations: (1) By methods in use in this country (England) oxygen is practically excluded and were oxygen admitted together with nitrous oxid, it is possible, as our present knowledge tells us, that the oxygen would not be ousted by the nitrogen compound, and (2) what is the effect that nitrous oxid has upon the elimination of carbonic acid gas from the lungs?

"(1) The deprivation of oxygen leads to asphyxia, pure and simple, for if a person respires in an atmosphere of nitrogen, although all carbon dioxid diffuses out, yet asphyxial symptoms, hyperpnea, dyspnea and convulsions appear; (2) nor does nitrous oxid, in any way, interfere with the elimination of carbon dioxid from the lungs. Careful experiments have shown that nitrous oxid affects carbon dioxid elimination in only an indirect way. During the cutting off of the oxygen supply tissue metabolism is greatly lessened and as a consequence the production of carbon dioxid is decreased, so that in this case the diminished elimination is merely an indication of lessened production. We find a marked similarity between the tissues rendered stagnant by nitrous oxid and the sluggish behavior of organic matter in animals during hibernation. At the same time there is a fairly active carbonic acid elimination, as much in fact as represents tissue waste, during the period of anesthesia, and this carbonic acid, in the absence of recuperative oxygen, is, I submit, an important fact requiring our attention when we have to take into consideration the practical lessons taught by the physiology of nitrous oxid. In this connection it seems consistent with these lessons to insure the removal of carbon dioxid so that the patient may not breathe nitrous oxid polluted with an excess of it.

"We may then take it that the blood is capable of acquiring nitrous oxid by simple absorption and probably by the union of that gas with the albumenous matter in the liquor sanguinis and corpuscles. No attempt has as yet succeeded in demonstrating the conjunction of nitrous oxid with hemoglobin, at least no crystalline forms; such as we are cognizant of, have been found. However, nitrous oxid possesses a strong affinity for the salts of iron, so that it is perhaps not unwarrantable to suppose that the iron containing hemoglobin should readily unite itself in actual chemical union with nitrous oxid. But nitrous oxid can, as we have pointed out, actually oust oxygen from its absorption, and with great rapidity become immediately associated with some of the blood constituents, in order that it may be wafted with extraordinary rapidity to the nervous center, there to bring about the profound change in nerve tissue, which is evidence externally by the anesthetic coma of nitrous oxid narcosis.

"Spectroscopic researches of the blood impregnated with nitrous oxid do not effect conclusive evidence of value. McMunn failed to obtain any characteristic spectrum from the blood of animals poisoned with nitrous oxid.

Personally, I have repeatedly made attempts to obtain a spectrum peculiar to this agent, but have always been unsuccessful. The only bands discernible being the broad ones between Fraunhofer's D and E lines, which of course merely represent spectrum. Dr. Halliburton, Assistant Professor of Physiology in University College, was good enough to examine some blood for me, and he concurs in my results. Now this negative evidence cannot be taken as sufficient for us to base any conclusions which deserve to be reckoned final."

CHADBOURNE AND LEUCOCYTOSIS.

Chadbourne,[7] in the study of 21 cases found that there was an increase in the number of leucocytes per cubic millemeter following anesthesia. In this series of cases counts were made immediately after ether had been continued for a period of 16 2-3 minutes. The average increase in the number of leucocytes was found to be 37.3 per cent., (the lowest 6 per cent., the highest 73 per cent.) Chadbourne made differential counts in five of his cases, (Table 1,) and found that this increase affected both the polymorphonuclear cells and the lymphocytes to an equal degree.

BLOOD EXAMINATIONS IN RELATION TO ANESTHESIA AND OPERATIONS.

Hamilton Fish,[8] has contributed an extremely valuable article on this subject. He not only affirms that ether reduces hemoglobin and affects red corpuscles, but he also believes that anesthesia lessens tissue resistance and thus leads to septic lesions; and he considers the condition of the blood as a fairly accurate guage of the patient's general condition and that the blood. should be examined before the administration of an anesthetic. *He maintains that those afflicted with neuresthenia, anemia, chlorosis, leukemia and the lymphatic temperament have blood in which marked changes can be demonstrated and that all these patients stand operations and anesthesia badly. Fish advocates the view that the anesthetic extracts oxygen from oxyhemoglobin and is taken away from the corpuscles, which are so poor in that element, that they cannot spare it. As a consequence such corpuscles are unable to give any oxygen to the tissues and these patients under the influence of ether will show evidence of collapse. Fish also reminds us that respiration depends on the integrity of the nervous system and upon the amount of hemoglobin in the blood, and that if hemoglobin is reduced below a certain limit, respiration ceases.* He thinks this minimum to be about 20 per cent. and refers to the observations of Miculisz, that in three cases dying of collapse during the operation, only 15 per cent. hemoglobin was found remaining in the blood. In Fish's opinion the safest rule is not to give a general anesthetic if hemoglobin is under 50

TABLE I

Differential Leucocyte Count After Ether Anesthesia

No.	Before	After	Percentage of Increase	Time Mins.	Number of Leucocytes counted				
					Type	Before	After	Before	After
9	21,290	27,220	23	0.25	Polyn. Mono. Eosin.	83.8% 14.6 0.2	82.4%	500	500
13	7,600	13,150	72	0.18	Polyn. Mono. Eosin.	71.1 28.3 0.5	69.4 30.5 9.1	1,000	1,000
14	12,950	20,690	21	0.12	Polyn. Mono. Eosin.	69.8 23.2 0.2	30.5 29.8 0.4	500	500
15	12,350	21,360	73	0.18	Polyn. Mono. Eosin.	82.8 16.0 1.2	77.6 21.6 0.8	500	1,000
18	14,000	17,000	21	0.15	Polyn. Mono. Eosin.	83.2 13.8 0.4	85.8 13.8 0.4	1,000	500

per cent., while anything above 80 per cent. he considers normal. The amount of anesthetic which is harmless in the presence of 80 per cent. hemoglobin may be extremely dangerous to life when the hemoglobin content is reduced to 50 per cent. He also points out the importance of the fact that safe anesthesia depends not only on a good percentage of hemoglobin but also upon the presence of a normal or an increased number of polynuclear neutrophiles. He regards the leucocytosis of anesthesia as phagocytic in character and as an indication of individual resistance. He believes that the blood should be examined not only before but also during anesthesia; because the first evidence of impending danger may be found in the blood change. He also emphasizes the interesting fact that at an altitude of one mile above sea level, hemoglobin is reduced from 12 to 15 per cent. during the first hour of anesthesia.

Bloodgood,[9] in reviewing Fish's article, entirely agrees with the author's conclusions and cites several cases occurring in the Johns Hopkins Hospital to confirm these views.

DACOSTA AND KALTEYER'S CONCLUSIONS.

DaCosta and Kalteyer,[10] made a very exhaustive study of the blood during ether anesthesia by making counts of the red blood cells and readings for changes in the hemoglobin content of 50 patients. Their summary and a table of averages are included in the paper and are as follows:

"(1) Etherization produces diminution of hemoglobin in the blood. (2) Red corpuscles and hemoglobin are especially affected in blood previously diseased. (3) Irregular records are due to faulty observations, to the presence of altered hemoglobin in the blood, to faulty alteration as to color of a V. Fleischl instrument or to taking blood for examination before anesthesia is complete. (4) White corpuscles show irregular changes, which are not characteristic and exhibit variations more pronounced than would be found in the same number of samples of normal blood on different examinations. (5) Age does not influence results. (6) Prolonged anesthesia profoundly deteriorates the blood and strongly militates against recovery, hence rapidity of operation is most desirable. It is a generally accepted fact that ether causes leucocytosis. Anesthesia may also lessen tissue resistance and lead to sepsis. (7) The blood is a fairly accurate guide to the patient's condition and should always be examined before the administration of an anesthetic, for the anesthetic may probably extract oxygen from the oxyhemoglobin and combine with hemoglobin.

TABLE II

Blood Changes Induced by Ether Anesthesia.
(DaCosta-Kalteyer)
Averages of Fifty Cases Examined.

	No. Cases	Corpuscles	Color Index	Hemoglobin%
Before Anesthesia	50	4,977,440	0.903	89%
After Anesthesia	50	5,126,000	0.821	86
Difference	50	149,660 plus	0.082 minus	3 minus

EXPERIMENTS OF BOSTON AND ANDERS ON THE HUMAN SUBJECT AND RABBITS.

The experiments of Boston and Anders,[11] differ from all others in that they took a healthy man, free from purgatives and hired him to take ether from which their conclusions were drawn in corelation with experiments on five rabbits. They report differential counts during anesthesia and these tables are added to their report, which follows:

"Our experiments on animals show that the hemoglobin was reduced in every instance as a result of ether anesthesia. The hemoglobin content reaches its lowest point in from 24 to 36 hours after ether anesthesia. It was a rule for animals to display a less decided loss of hemoglobin during the second or third etherization, than at the first ether narcosis.

"In the human subject the reduction in hemoglobin was no less decided than in rabbits; one-half or more of the fall in coloring pigment taking place during the first 20 minutes of the anesthetic state. Polycythemia was always found to be more or less the direct result of cyanosis. Changes in the red cells as the result of ether anesthesia, were always present and the blood was found to flow slug-

gishly from the site of puncture; the individual cell seemed compact and its edges thickened. The central biconcavity was often obliterated from such cells. Small streaks and irregular patches of pallor were seen disseminated over the surface of many of the red cells and outlined areas from which the hemoglobin had been extracted. Neucleated erythrocytes were also occasionally found. Differential leucocyte counts were never found to show any points either of interest or value. In the human subject it was found that an increase from one-third to double the number of leucocytes followed ether anesthesia in one class of cases, this change taking place during the first 20 minutes of anesthesia.

J. H., male, age thirty-three, apparently in good health, was given ether without previous purging.

1. (*Before ether.*) The red blood cells were 4,080,000; leucocytes, 7,600; hemoglobin, 86 to 95 per cent., several estimates being made with different instruments. Stained blood was in every way normal.

2. (*Under ether twenty minutes.*) The red blood cells were 6,150,000; leucocytes, 16,000; hemoglobin, 79 per cent. No poikilocytes; microcytes numerous; no macrocytes found. All cells stained palely but evenly throughout. White cells showed an increase in the polynuclear elements.

3 (*One hour after ether.*) The red blood cells numbered 8,220,000; hemoglobin, 74 per cent. An increase of 2,070,000 cells per cmm. From the degree of cyanosis present it is fair to attribute a liberal portion of this increase to this condition. Hand-in-hand with an increase in the number of red cells there was a loss of 12 per cent. in the hemoglobin. It is at once apparent that 74 per cent. of hemoglobin is an extremely low amount for a blood of such condensation, and that each red cell is extremely poor in coloring pigment. Leucocytes, 9800. The leucocytes which rose from 7600 to 16,000 during the first twenty-five minutes, had now dropped to 9800, despite the extreme degree of blood concentration.

Studying these figures correlatively, one is forced to believe that a true leukemia existed. Occasionally cells were seen which stained deeply, no crenated cells. Decided variations in size of cell.

Differential count of leucocytes.

	Per cent.
Polymorphonuclear cells,	80.97
Myelocytes,	4.27
Transitional cells,	11.00
Large mononuclear cells,	1.11
Small lymphocytes,	2.22
Eosinophiles,	0.43
	100.00

4. (*Twenty-four hours after ether.*) There had been no vomiting, and the patient had taken food and claimed to feel well. The red blood cells were 4,576,000; leucocytes, 13,600; hemoglobin, 67 per cent. (loss of 19 per cent.). In the stained specimens were seen many macrocytes, many of which stained poorly, some only as shadows, and these were liable to be distorted (poikilocytosis). Leucocytes mostly large mononuclear and polymorphonuclear forms.

5. (*Thirty hours after ether.*) The red cells were 4,600,000; leucocytes, 12,000; hemoglobin, 78 per cent. (increase of 11 per cent. in six hours.)

6. (*Forty-eight hours after ether.*) The red cells were 5,700,000; leucocytes, 10,600; hemoglobin, 80 per cent. There was an appreciable increase in the polymorphonuclear elements and in small lymphocytes. Two myelocytes were found. Eosinophilic myelocytes were also present. Some of the cells stained irregularly, but there were no pale cells as previously seen.

7. (*Seventy-two hours after.*) The red cells were 4,780,000; leucocytes, 7400; hemoglobin, from 85 to 86 per cent.

Second etherization:

8. (*Before ether*—patient not purged.) The red cells were 5,005,000; leucocytes, 6700; hemoglobin, 80 per cent. The stained blood appeared perfect in all respects.

9. (*Under ether twenty minutes.*) The red cells were 5,310,000; leucocytes, 8200; hemoglobin, 74 per cent. A few megaloblasts were present, but there was practically no distortion of the red cells; microcytes were few; all red cells stained perfectly; white cells in about normal relation, except for a slight apparent increase in the eosinophiles.

10. (*Under ether forty minutes.*) The red cells were 5,250,000; leucocytes, 12,000; hemoglobin, 77 per cent. (Ether discontinued.)

11. (*One hour after starting ether.*) Perspiration free and slight vomiting. The red cells were 5,120,000; leucocytes, 15,000—the gradual rise continued, reaching its maximum number at this stage; hemoglobin, 72 per cent.

12. (*Six hours after ether.*) The red cells were 4,430,000; leucocytes, 11,000; hemoglobin, 63 per cent. (a loss of 17 per cent). Vomited four or five times in the afternoon.

13. (*Twenty-four hours after ether.*) The red cells numbered 3,820,000; leucocytes, 5700; hemoglobin, 63 per cent.

14. (*Forty-eight hours after ether.*) The red cells numbered 3,820,000; leucocytes, 5700; hemoglobin, 70 per cent.

15. (*Seventy-two hours after ether.*) Vomited twice, and there had been moderate sweating. The red cells numbered 5,747,000; leucocytes, 8250; hemoglobin, 73 per cent.

16. (*100 hours after ether.*) Vomited yesterday and this morning; frequent perspiration, anexoria, and constant drowsing. The red cells numbered 3,920,000; leucocytes, 6000; hemoglobin, 76 per cent.

THE EXPERIMENTAL RESEARCHES OF HAMBURGER AND EWING.

Hamburger and Ewing,[12] in 1907, made one of the most exhaustive researches into the problems of this subject and their conclusions are very valuable from the fact that they were drawn from experiments on man and animals with chloroform, ether and nitrous oxid. It is pertinent that their conclusions should be included in this review and the tables accompanying them, showing the curves and changes in hemoglobin, erythrocytes and the color index. No record is found of their having

made differential counts. Their conclusions are:

"(1) In an analysis of the blood changes incident to *nitrous oxid* anesthesia in a series of clinical and chemical observations, we find that: (a) the hemoglobin is not permanently reduced nor is anemia produced; (b) hemolysis is not increased; (c) the changes in the readings of hemoglobin and erythrocytes are transient and of no surgical significance and are most likely to be explained on the basis of capillary stasis. The production of reduced hemoglobin is not a result of the anesthetic itself, but is due to the accompanying asphyxia; (e) the changes in the coagulation time are not constant, but in general there is an increase in the time required for clotting, most marked about the third day.

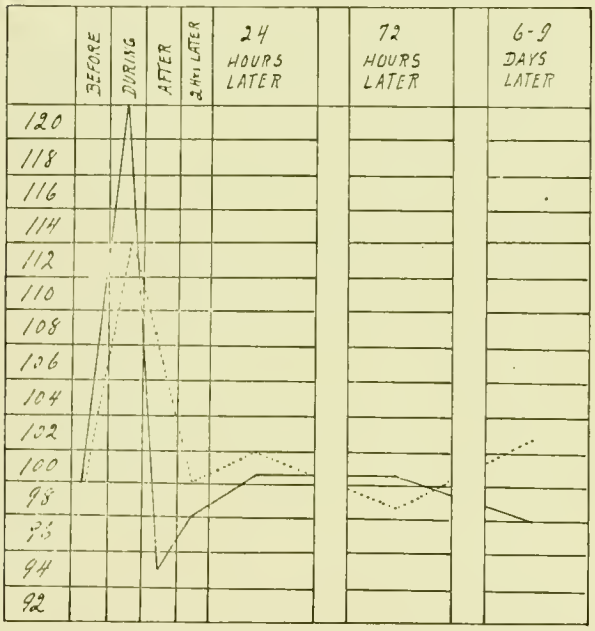


Chart iii. Curve showing the effect of nitrous oxid on hemoglobin (solid line) and erythrocytes (broken line).

"(2) In an analysis of blood changes incident to *ether* anesthesia in a series of experimental observations, we find that: (a) the hemoglobin is slightly reduced and therefore slight anemia is produced; (b) hemolysis is not materially increased; (c) changes in the hemoglobin and erythrocytes are to be explained on the basis of blood inspissation; (d) ether causes a marked decrease in the coagulation time of the blood most marked from 7 to 10 days after ether anesthesia.

"(3) In an analysis of the blood changes incident to *chloroform* anesthesia in a series of experimental observations on animals, we find that: (a) the hemoglobin is reduced and therefore an anemia is produced; (b) hemolysis is increased; (c) chloroform causes a slight decrease in coagulation time, most marked from the 7 to 10 days after chloroform anesthesia.

"(4) *In a comparison of the three anesthetics from the standpoint of the changes in the blood, we conclude that nitrous oxid has no permanent effects of any significence; that ether causes more harmful changes, (slight anemia and marked decrease in the coagulation time); that chloroform causes the most harmful results, (hemolysis and the production of distinct anemia).*

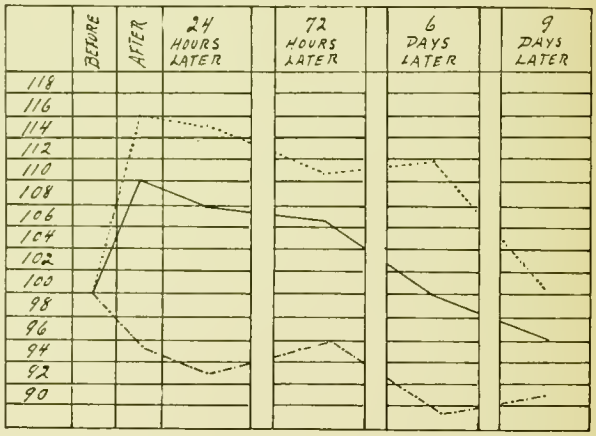


Chart iv. Curve showing the effect of ether on hemoglobin (solid line), erythrocytes (broken line) and color index, (dot and dash line).

More recently W. L. Mendenhall,[13] working in the laboratory of the Harvard University Medical School has pursued the investigation of the "Influence of Certain Anesthetics on the Coagulation Time of the Blood," and as he has gone deeply into the physiological basis of the subject, his work is herewith given in considerable detail and some charts of comparative coagulation time curves of chloral, chloroform and ether are included. Mendenhall reports as follows:

"Cannon and Gray have presented evidence

that injections of adrenalin result in a hastening of the coagulation time of the blood. Other evidence by Cannon and Mendenhall has shown that stimulation of the splanchnic nerves produces a like effect upon coagulation time. Several investigators, notably Dreyer, Tscheboksaroff, Asher, Kahn, Meltzer and Joseph, Elliott, Cannon and Lyman, have shown that artificial stimulation of the splanchinc nerves leads to a discharge of adrenalin into the blood. Also it has been proven that certain emotional reactions such as fear and rage, occurring in the normal life of an animal, induce a discharge of adrenalin. This latter effect has been proven to be due to the passage of impulses along the splanchnic

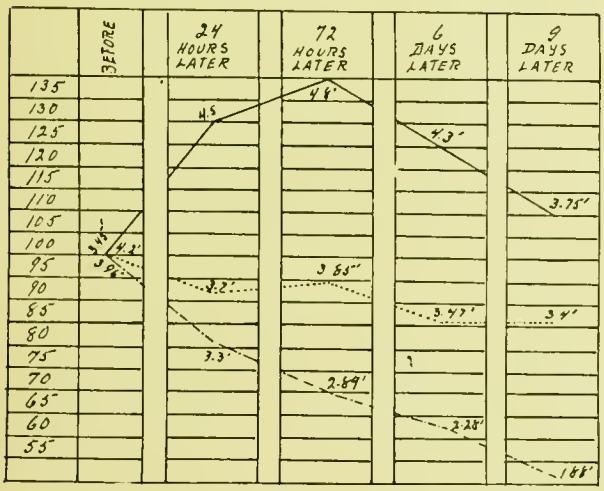


Chart v. Curve showing the effect of chloroform on hemoglobin (solid line), erythrocytes (broken line) and color index (dot and dash line).

nerves. Elliott has shown that the adrenalin content of the adrenal gland is reduced by the administration of various anesthetics; and that this effect with ether and chloroform is due to stimulation of the suprarenal glands through the splanchnic nerves. The experiments of Olivia have not only corroborated Elliott's but have shown that chloroform discharges the adrenal glands more completely than does ether; and also that the adrenalin content is more quickly regained after ether than after chloroform anesthesia.

"The question of the effect of anesthetics upon coagulation time has long been of prime importance to both surgeons and obstetricians. Their chief concern, however, has been in the after-effects as agents productive of postoperative or postpartum hemorrhages. Chloroform seems to be the one most often recognized as causing a change in the coagulation process. Whipple and Hurwitz recently have shown that several hours after adminis-

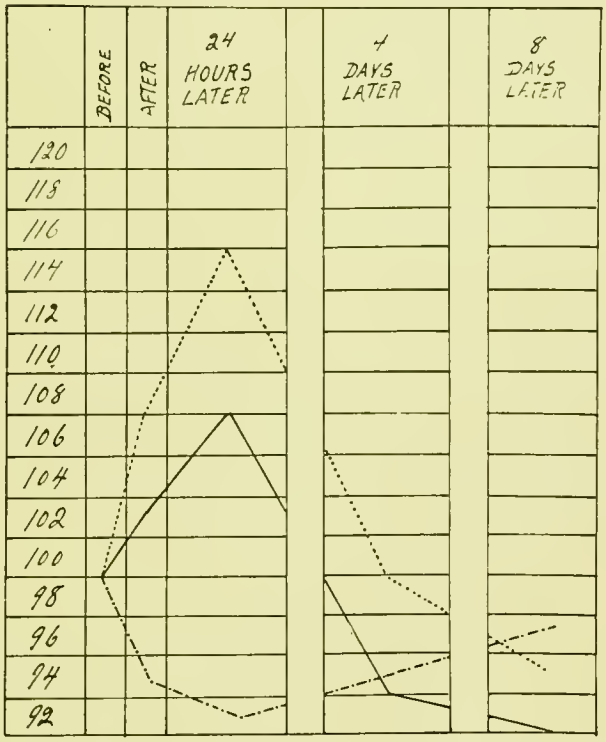


Chart vi. Curve showing the effect of nitrous oxid (solid line), chloroform (broken line) and ether (dot and dash line) on the coagulation time of blood.

tration of large doses of chloroform to dogs the coagulation time is unchanged; they call attention, however, to the weak consistency of the clots. They ascribe the cause of postoperative hemorrhages following administration of chloroform as a failure of the clot to hold firmly rather than a retardation of clotting processes. That the liver is concerned in the coagulation of blood has been shown by many observers.

"The foregoing evidence led to the question of the effects of ether and chloroform upon blood coagulation during the administration of the drugs. Inasmuch as previous experi-

ments were concerned with immediate factors affecting coagulation time it was thought logical to study the immediate effects of ether and chloroform upon the coagulation process. These drugs, furthermore, have been shown to exert action upon organs that are intimately involved in blood coagulaton, *the liver and adrenals*. It was hoped, if changes occurred during anesthesia by these drugs, that such changes might be of value in studying their after-effects or in explaining after-effects of this form of anesthesia upon coagulation time, and also that they might throw some light upon the complex of organs involved in the coagulation mechanism.

"Decerebrate animals (cats) were used throughout this investigation. Two reasons led to the adoption of this type of animal; first, the animals of the whole series were placed under practically uniform conditions, and second, the animal was free from the anesthetic whose action it was desired to study. It was necessary in the beginning of each experiment to induce anesthesia for a short time in order to perform decerebration. Ether was used therefore in the beginning of the experiment. Care was taken to produce not too profound anesthesia and to remove the cerebrum as quickly as possible after beginning the administration of the ether. The usual routine was as follows. Simultaneously with securing the animal on the board the ether was applied with a cone, and the neck was prepared by clipping the hairs. By this time anesthesia was deep enough to permit operative procedures. The animal was then tracheotomized, a tracheal cannula inserted, and both carotids tied. Then it was turned over and decerebration performed according to the method of Forbes and Sherrington. The total time elapsing from the application of ether to its removal never exceeded fifteen minutes, usually it was from ten to twelve minutes. After decerebration the femoral artery was prepared for withdrawal of the blood. The temperature of the animal was maintained when necessary by an electric heating pad. A thermometer was inserted into the rectum. The ether or chloroform was given by means of the bottle used in ordinary laboratory operations. It consisted of a small bottle of about 75 cc. capacity. It was stoppered by a rubber cork through which passed two right angle glass tubes, each 1 cm. in diameter. One of these tubes conducted air to the surface of the anesthetic; the other conducted the ether-air mixture to the animal by means of a short rubber tube connected to the tracheal cannula. This rubber tube had an oblique cut in the wall so that by shifting the bottle more air could be mixed with the ether if the animal showed signs of asphyxia. The corneal reflex was used to determine if anesthesia was present; also vibrissae, ear and tail reflexes were used. After all operative procedures were finished the animal was left undisturbed for forty-five minutes or an hour. This was done in order that the animal might be free from ether when observations were to be made, and also because of the discovery that operative procedures may shorten the coagulation time. It was felt that the time mentioned above sufficed to free the animal from the preliminary small dose of ether and also any hastening factor that may have been aroused by operations. All experiments began with observations taken at intervals of ten minutes for forty minutes or an hour to determine the normal coagulation time of the animal, then anesthesia was induced by the means described above and observations continued every ten minutes for an hour.

"A total of sixty-three successful experiments were performed. Preliminary to the investigation of chloroform a number of experiments were made with chloral hydrate. It was thought that this drug would give some valuable data which would be indicative of the action of the whole series of chlorin containing anesthetics. Moreover it might reduce the number of animals which would be necessary for the study of chloroform. Thus the fatalities resulting from the powerful toxicity of the chloroform would be reduced. In actual experience the fatalities due to chloroform were surprisingly small. Inasmuch as chloral hydrate is frequently used for its anesthetic effect, the study of its influence on coagulation time is not without value.

THE EFFECTS OF CHLORAL HYDRATE ON BLOOD COAGULATION TIME.

A total of 23 experiments were performed with chloral. The doses were given intravenously, the injection time being between 3 and 5 minutes. The dose varied from 65 to 100 mgm. per kilogram. The results of these experiments reveals the curious facts that the effect which chloral hydrate has upon coagulation time bears a distinct relation to the coagulation time *before chloral was administered*. Thus if the normal coagulation time was 6.8 minutes or less chloral *prolonged* the coagulation; whereas, if the normal coagulation time was 6.9 minutes or more, then chloral *decreased* the coagulation time.

Chart vii, A, is a composite curve based upon the results with chloral. The straight line at the beginning of the curve represents the average normal coagulation time. The ordinates represent minutes of time for coagulation to occur. The abcissae represent intervals of five minutes from the time when the drug was given. The general average of these experiments showed a normal coagulation time of 6.2 minutes. After chloral was administered the average coagulation time increased 4.8 per cent.

Chart vii, B, is a curve constructed in a similar manner. In this curve only those experiments were used whose normal coagulation time was 6.8 minutes or less. It is to be noted that only once did the coagulation time fall below normal and then only 0.1 minute. The curve shows the striking effect that chloral has upon a short coagulation time. The average increase in coagulation time as shown hy this curve amounted to 28.2 per cent.

Chart vii, C, is a curve composed of those experiments whose normal coagulation time was decreased in these observations. The average decrease amounts to 7.5 per cent., which allowing for a leeway of 6 per cent. error, makes this decrease negligible in comparison with the increase. The fact that chloral exerts its retarding effect more when a short normal is present, suggests the idea that it acts antagonistically to hastening factors present in the blood or that it may depress activity of organs which produce or activate hastening factors. The action of chloral on the liver is well known. No reference is available, however, in regard to its effects on the adrenals. The weight of evidence obtained in these experiments shows that chloral hydrate, if it affects the coagulation time at all, tends to prolong it. The prolonga-

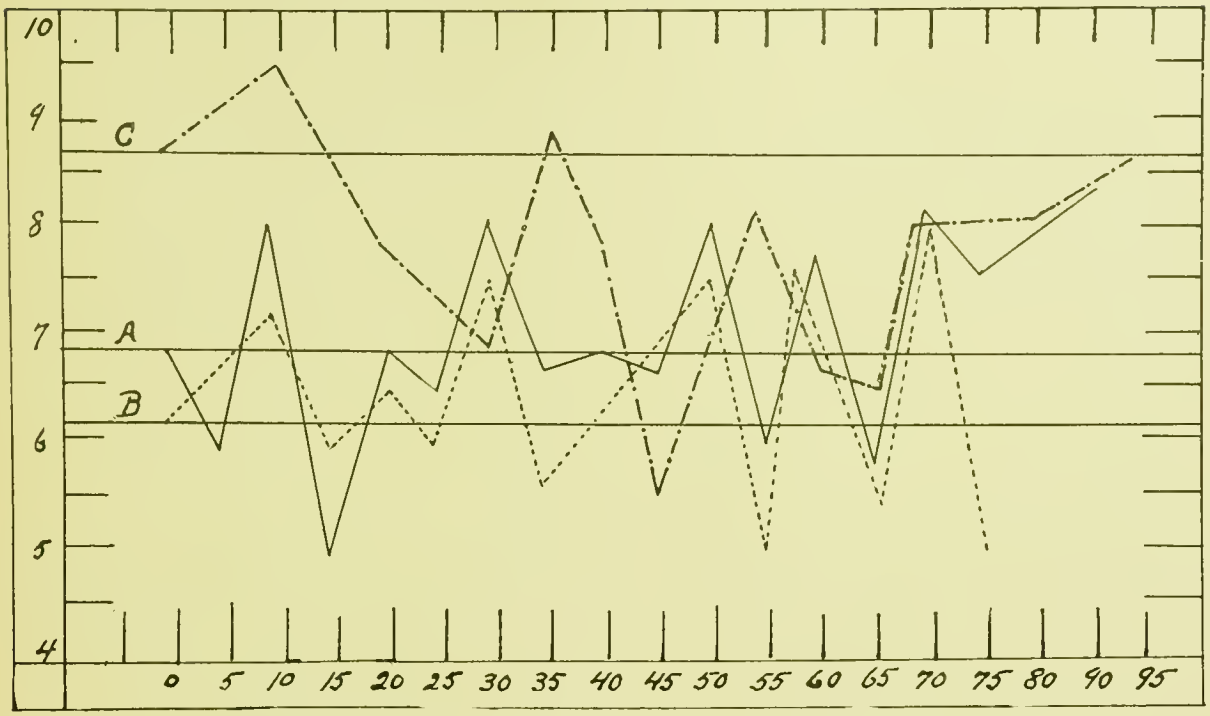
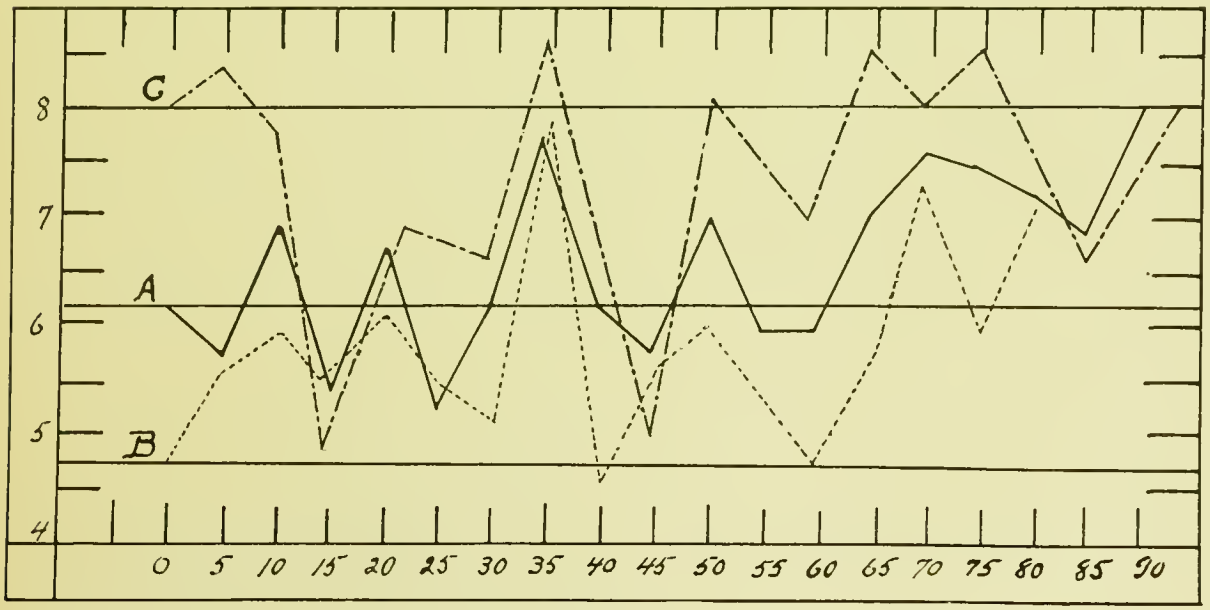


Chart vii. Curves showing the coagulation time of the blood as effected by chloral hydrate. A, normal; B, short, and C, long.

Chart viii. Curves showing the coagulation time of the blood as effected by chloral hydrate. A, normal; B, short, and C, long.



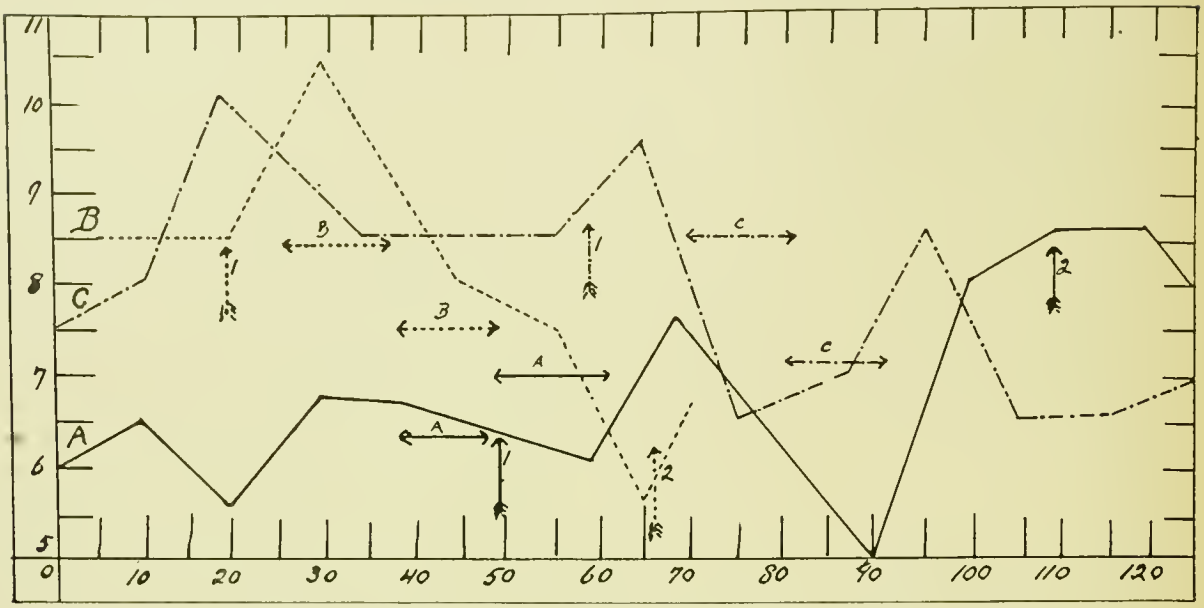
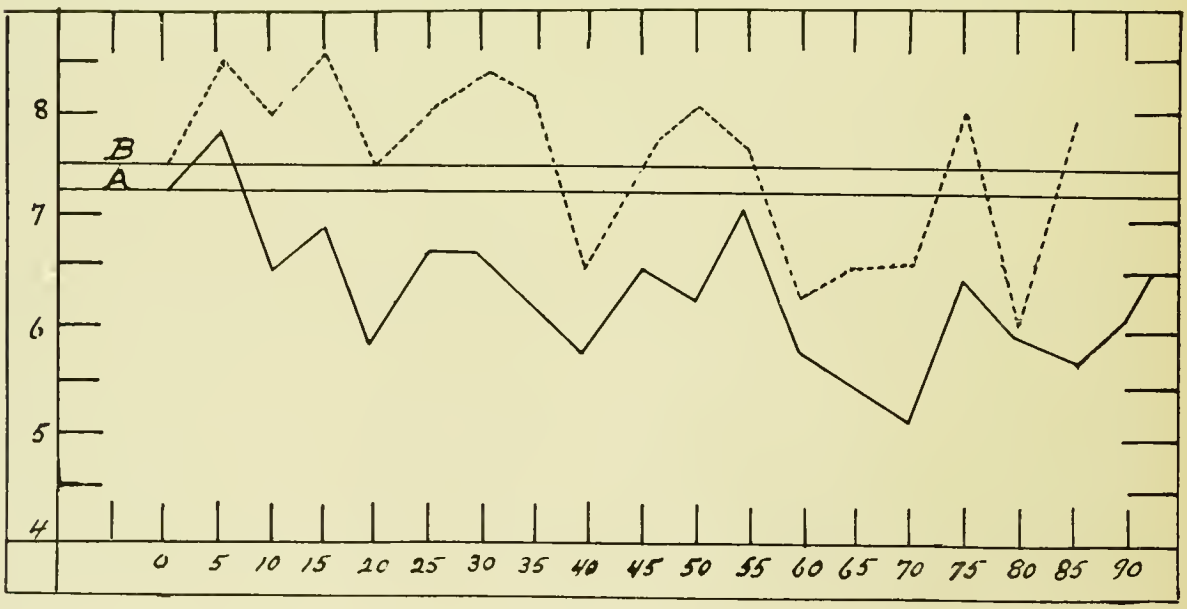


Chart ix. Curves showing effects of chloroform and ether on coagulation time. A and B, chloroform given at 1 and removed at 2. Horizontal arrows, (solid and dotted) represent averages before and after chloroform was given. C, similar averages for ether (dot and dash line).

Chart x. Curves showing the coagulation time of the blood as effected by ether. A, adrenal glands intact; B, adrenal glands removed.



tion is greater when the normal coagulation is short. The evidence does not warrant a conclusion that retarding factors are produced.

EFFECTS OF CHLOROFORM ON BLOOD COAGULATION TIME.

Fifteen experiments were performed with chloroform. The amount of chloroform used varied somewhat, the average being 10 cc. Anesthesia, as noted by reflexes, was usually complete in from 3 to 4 minutes. Chloroform behaved similarly to chloral hydrate, thus if the normal coagulation time was short, chloroform prolonged it, whereas, if it was long, a decrease resulted. In these experiments, as in those with chloral hydrate, a composite curve shows little effect of the drug, except to make the coagulation time irregular. *A curious fact is noted in the point where chloroform action changes from an increase to a decrease of coagulation time. It occurs at 7.5 minutes, with the chloral hydrate it was 6.8 minutes, a difference of less than a minute.* Chloroform is known to affect two organs that are important in coagulation processes—the liver and adrenals. It would be natural to suppose that its effect at any one time upon coagulation would depend on various interrelations among many factors. If the adrenals were discharged completely, it might still exert an effect upon coagulation time by disturbing liver function; or if the adrenals were highly charged, the resulting outpour might, or might not be effective because of an impairment of liver function. Chart vii, A, B, C, are composite curves for chloroform experiments with normal, short and long coagulation time. *The increase under chloroform is more noticeable about an hour after the beginning of anesthesia. Previous to the increase there may be evidence of a disturbance of balance between opposing forces with a final predominance of the factors that retard coagulation or perhaps a decrease in effectiveness of hastening factors. After chloroform is removed the hastening factors again appear.*

EFFECTS OF ETHER ON BLOOD COAGULATION TIME

A total of 21 experiments were performed with ether. 13 were made with the adrenals intact and 8 with the adrenals removed. An average of 50 cc. of ether was used in each experiment. With the adrenals intact in no instance did ether increase the coagulation time, Chart x, A; nor was there any distinct relation between normal coagulation time and the effect of ether. The consistent action of ether suggested the idea that only one factor of coagulation, the hastening factor was affected. Since Elliott was shown that ether discharges the adrenal gland it was thought desirable to remove the adrenals and see if adrenalin, was the factor which was affected. In Chart x, A, in which the adrenals are intact, the average percentage decrease with the adrenals removed was 1.3 per cent. The evidence shows therefore that ether decreases the coagulation time and that the effect is exerted through the adrenal gland.

SUMMARY.

The observations in these experiments seem to warrant the following conclusions:

(1) Coagulation time is little altered by chloral hydrate unless it is normally short, then it is prolonged.

(2) Coagulation time is affected by chloroform as by chloral hydrate,—if the process is affected at all it more usually prolonged rather than hastened.

(3) The effects of chloral hydrate and chloroform are probably the result of disturbances and consequent interactions between two or more organs which are important in the coagulation process, probably the liver (intestines?) and adrenal glands.

(4) The evidence is not sufficient to prove that a retarding agent is produced.

(5) Coagulation processes are hastened by ether anesthesia.

(6) The effect of ether on coagulation is exerted wholly through its action upon the adrenals.

Working in the Cushing Laboratory of Experimental Medicine, Western Reserve University and Lakeside Hospital, Cleveland, M. L. Menten and George W. Crile[14] have, during 1915, published their experimental data and clinical observations on "The H-Ion Concentration in Blood under Various Abnormal Conditions." As the H-ion content is coming into prominence as a diagnostic and prognostic factor in operative and anesthetic risks, the contentions of Menten and Crile are given in full.

"Since the application by Höber in 1900 of the Nernst hydrogen concentration chain to the measurement of the reaction of the blood, our knowledge of that subject has been greatly extended. Irrespective of the methods used all the results published reveal the fact that the reaction of normal blood lies within comparatively narrow limits, although Hasselbach and Michaelis have noted that venous blood is always slightly more acid than arterial blood, due, probably, to the greater carbon dioxid tension in the former. Even the investigations of blood in pathological conditions, where acidosis occurs, have failed to show any considerable deviation from the recorded narrow limits, and only in diabetes where deep coma has been reached, does there occur any demonstrable increase in the H-ion concentration of the blood, although oxybutiric and diacetic acids are known to be produced in not inconsiderable amounts in that disease. The only remaining condition in which an increased acidity of the blood has been observed is that of narcosis reported by Michaelis.

METHODS

"The H-ion concentration in our experiments was measured by the method of Michaelis. All measurements were made on animals at laboratory temperatures varying from 18p° to 24°C., and for these variations corrections were made, the quantities of blood used from 2.5 to 3. cc., were diluted to 6.5 cc. with 0.85 per cent. sodium chlorid containing hirudin in solution. When possible the blood was allowed to drop directly into the electrode from the ear of the animal employed in other cases a cannula was inserted in the vessel and the blood passed from this into the electrode.

RESULTS AND DISCUSSION

"In some of our earlier estimations of the H-ion concentrations of the blood it was observed that in anesthetized animals the acidity of the blood was considerably higher than that reported from normal animals. A systematic study was then made of the blood of animals anesthetized with chloroform, ether and nitrous oxid. For these experiments dogs and rabbits were used because of the comparative ease in obtaining blood from the ear blood vessels of these animals. The blood was bled from an incision in the blood vessel of the ear directly into the electrode; the same animal was then anesthetized and blood again taken from the same site in a similar manner so that in every case the blood in anesthesia could be compared with the normal blood of the same animal.

"In a large number of experiments the values obtained for normal blood showed a wide variation, ranging in the dog from pH—7.64 to pH—7.32. In the rabbit the variations were even more marked, the minimal and maximal figures obtained being pH-7.18 and pH-7.70, a phenomenon which will be discussed later.

"Under the influence of the three above mentioned anesthetics, when anesthesia reaches the stage in which reflexes are completely abolished, the reaction of the blood measured at 20 C. may fall to pH-7.00. As far as could be ascertained in our experiments *the degree of acidity produced depended solely upon the amount of the drug inspired. The deeper the anesthesia the more marked the acidity, (pH—7.00 to pH—7.60) and vice versa; although prolonged duration of anesthesia is not a factor in increasing the H-ion concentration of the* blood. Further, the increase in acidity commences as soon as the anesthetic enters the circulation, and a diminution takes place immediately on the cessation of the administration of the drug, until 45 minutes subsequently the blood again resumes its normal H-ion concentration.

"Narcosis produced by morphin, even when this drug is given in such large doses as 75 cc. of 1 per cent. morphin sulphate in two hours, fails to reveal any demonstrable changes in H-ion concentration. Alcohol, however, seems to induce an acidity that persists for hours after administration. Also in several operative cases in the Crile clinic measurements of the H-ion concentration during nitrous oxid anesthesia showed the blood reaction to be respectively pH—7.20 and pH—7.22.

"Not only in anesthesia but also in other abnormal states the blood reaction was observed to become more acid. The most striking of these was *fright*, a phenomenon remarkably shown in the rabbit. Ordinarily, if blood is taken from the ear of a rabbit, so that the animal is disturbed as little as possible, the blood shows a fairly high alkalinity. Under the influence of fright this is altered, in an astonishingly short time and to a most profound extent. Another noteworthy feature is the rapidity with which blood regains its normal reaction. Similar observations regarding such marked effects of fright have been very rarely observed by us in dogs.

"Since the stimulus of fright can produce such a prompt and intense response it is to be surmised that in other emotional disturbances similar changes in acidity may be encountered. Experiments to test this supposition were made for *anger* in cats and it was found that the expression of that emotion is also accompanied by profound changes in the blood of the animal.

"The possibility that the cause of the increased acidity was an accelerated oxidation with the accumulation of its accompanying products in the circulation led to the estimation of the blood reaction during and immediately following *insomnia*, where it was thought the prolonged metabolic processes taking place, might give rise to a similar condition of the blood. But tests on a series of six rabbits, housed in a warm place, abundantly supplied with food and water and kept awake for 100 consecutive hours, were quite negative on this point.

"Evidence of a similar sort is also obtained in pitched animals, in which, immediately after the severing of the spinal cord there is a rapid rise of H-ion concentration, due undoubtedly to the decreased lung aeration and consequent faulty elimination of carbon dioxid, for on the establishment of artificial respiration, the normal reaction of the blood is promptly restored. When in such pitched animals, where a normal H-ion concentration is being normally maintained by artificial respiration, violent contraction of the skeletal muscles were produced by electrical stimulation of the cut end of the cord in communication with the musculature of the thorax, abdomen and extremities, no evidence of an increased acidity of the blood was found, except when the animal was dying.

"One other condition in which the blood showed an increased acidity was that of *shock*.

"In addition to the conditions above reported, where increased acidity of the blood obtains, is appended lastly a very interesting observation where a diminution of the hydrogen-ion concentration was noted; namely, in the blood flowing from the adrenal gland. In order to obtain blood which would contain, as far as possible, the maximal concentration of adrenal secretion, it was found necessary to clamp the adrenal vein just before it joins the vena cava, on the one side, and before it passes over the adrenal gland on the other side. The portion of the vein, between the clamps, therefore, lay directly over the gland and contained only blood from that organ. When this blood was withdrawn with a syringe and measured the value of the hydrogen-ion concentration was always from pH—0.10 to pH—0.12 lower than the blood taken from the immediately adjoining vena cava or from that part of the adrenal vein lying distal to clamp. While this difference is not large it is a very constant feature of adrenal blood. The assumption that this increased alkalinity is due to adrenalin is supported by the fact that the addition of adrenalin to blood serum, whose hydrogen-ion concentration is known, lowers it acidity and the diminution corresponds to the weight of adrenalin added when this is below the amount necessary for saturation. Thus if adding a definite amount of this substance, which as has been shown by Aldrich and others to be a very strong base, causes a certain increase in the hydroxyl-ion concentration, then when

twice or four times that amount is added the increase in alkalinity is multiplied by two and four respectively. Since at no time was it possible, with the apparatus used, to obtain blood from the vena cava, in the immediate vicinity of the opening adrenal vein which was appreciably more alkaline than blood from any other part of the vena cava, the adrenalin apparently causes a measurable modification of the blood in a very limited area. Moreover, that the influence of the adrenalin on the circulatory fluids is local in character is further evidenced by the fact that the removal of the gland caused no change whatever in the reaction of the blood until the animal was moribund. Although blood from the pancreas, liver and thyroid, as well as from the internal and external jugular veins was compared with blood from the vena cava of the same animal, no evidence of any variation in the H-ion concentration could be obtained. Further the removal of these organs singly or in combination caused no change in the reaction of the blood.

"The data presented in this paper proves conclusively that a very marked increase in the H-ion concentration may occur under certain abnormal conditions, and that the existence of this high acidity of the blood is not incompatible with life. As to the cause of the phenomenon and regarding its significance, the authors feel the present data to be too limited to warrant much speculation. Concerning the first point, however, one or two suggestions may not be amiss. The immediate and intense response of the blood to emotional stimuli by a marked rise in the H-ion concentration with the corresponding alteration of the character of respiration, and the rapid disappearance of these on the removal of the exciting cause, indicate that under these circumstances the carbon dioxid is a major factor; it is obvious however that all increased acidity of the blood cannot be ascribed to this source. This explanation does not suffice for shock and anesthesia, since in the former the carbon dioxid in the blood is markedly diminished as has been shown by Henderson and in the latter the carbon dioxid in the blood is increased according to the researches of Buckmaster and Gardner. Indeed in such a composite fluid as blood, containing so many complex chemical compounds, it is quite conceivable as has been suggested by Robertson that the amphoteric character of certain proteins must be of extreme importance in regulating the acidity of the blood."

SUMMARY.

(1) The H-ion concentration of the blood during certain emotional disturbances, such as fright in rabbits and dogs, and anger in cats, is markedly increased and at a temperature of 20 C., frequently reaches an acidity corresponding to pH-7.00. This is probably due to increased carbon dioxid tension.

(2) In anesthesia caused by ether, chloroform and nitrous oxid the H-ion concentration may be increased to the same extent. The change in acidity begins when the inspired anesthetic commences to react with the blood, and depends, approximately, on the degree of anesthesia. The restoration of the normal reaction of the blood is complete in 45 minutes after the administration of the anesthetic is discontinued.

(3) In two cases of shock the acidity of the blood was very much increased.

(4) The blood flowing from the adrenal gland is always more alkaline than venous blood elsewhere in the body. This increased alkalinity is local, not extending to any appreciable extent beyond the immediate vicinity of the adrenal vein, and is due to the dissolved adrenalin which it contains.

BLOOD CHANGES PRODUCED UNDER NITROUS OXID ANESTHESIA.

The following personal blood studies were made upon the human subject and confirmatory studies were also made upon tame and wild rats.

Physicians and nurses were selected as the human subjects for experiments to obviate, as far as possible, the elements of fear and anxiety and also to secure an enthusiastic and interested cooperation in furthering the contemplated researches. All the subjects chosen for experiments were free from alveolar abscesses and were to all intents and purposes in a normal, physical condition.

During the time that the subjects remained under the anesthetic, teeth were extracted, pulps removed or cavaties prepared for fillings, as indicated by the oral conditions presenting in the individuals at the time of operation. Hypodermic injections of analgesic or hypnotic drugs were never resorted to before the administration of anesthesia, in order not to complicate the problems involved. The blood required for study in each case was taken from the little finger of the left hand, a firm, small blood lancet being used for this purpose throughout the work.

The blood counts were taken immediately before the induction with nitrous oxid-oxygen anesthesia, immediately upon the return of consciousness and at intervals varying from 10 minutes to 3 hours after recovery of consciousness. The hematological examinations were made in Philadelphia Clinical Laboratory by Dr. E. Q. St. John and his associates.

A study of the accompanying tables will show that during anesthesia both the number of the cellular constituents of the blood and

the percentage of hemoglobin underwent a change from the normal in each particular individual. These changes were not always of equal importance, or in the same direction, but the tendency to increase or decrease followed certain definite lines. The general tendency of the *erythrocytes* was to decrease during anesthesia, an average loss of 16 per cent. being obtained in the eight cases studied; while the tendency of the *leucocytes* was to increase during anesthesia, an average gain of 16 per cent. resulting from the cases studied.

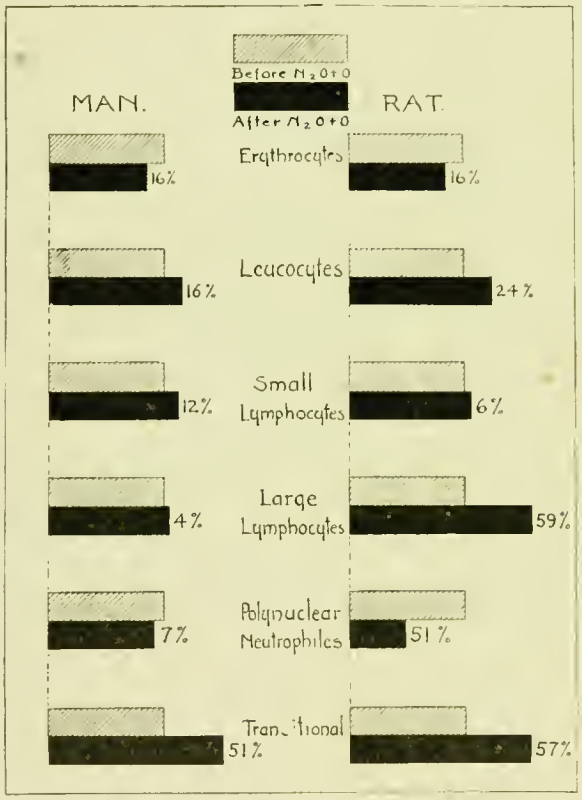


Chart xi. Percentage changes in the cellular constituents of the blood under nitrous oxid anesthesia in man and the rat.

Changes were also found to take place in the different varieties of leucocytes. There was found to be an average increase in small lymphocytes of 12 per cent; in large lymphocytes of 4 per cent. and in transitional forms of 16 per cent. An average decrease of 7 per cent. was found in the polynuclear neutrophiles. Poikilocytes, macrocytes, microcytes and nucleated cells were not observed at any time during the examinations. There was also a more or less pronounced reduction of hemoglobin throughout the entire series of cases and the coagulation time of the blood was decreased.

The following case reports show points of individual interests in the experiments on human subjects:

CASE 1. P., age 17, weight 97 lbs., blood pressure 132, diastolic 85, radial 68, slight mitral murmur. General appearance anemic. Nitrous oxid was administered for excavating several carious cavaties. Analgesia for 45 minutes, then anesthesia for 7 minutes for the extraction of three badly broken down teeth. The blood count taken just after the patient ceased to inhale the anesthetic showed a loss of 250,000 erythrocytes, and increase of 1,000 leucocytes and a decrease in the hemoglobin of from 82 to 77 per cent.

CASE 2. Miss B., aged 20, weight 120 lbs., blood pressure 110, diastolic 75, radial pulse 72. No excitement, analgesia with nitrous oxid-oxygen for 33 minutes, followed by complete anesthesia for 12 minutes. There was a desire to rest for some 25 minutes after recovery from the anesthesia. This patient had run the gamut of oculists, rhinologists, internists and serologists for relief of persistent headache. Spinal puncture had even been resorted to with only slight temporary relief. No cause for the condition was found in the teeth. Rest cure for hysteria proved unavailing and finally a radiograph showed a thickened condition of the occipital bone and the posterior portion of the parietal bone. This was diagnosed as the causative factor and the patient left without any hope of relief.

CASE 3. Miss R., age 23, weight 110 lbs., blood pressure 120, which rose to 130 under anesthesia; radial pulse 72. The patient was continually telling us, during a period of 50 minutes of nitrous oxid-oxygen analgesia, what a good time she was having in this case there was a loss of 250,000 erythrocytes and a marked increase of 3,000 leucocytes, the leucocytes returning to a normal count, or 5,550 in ten minutes after recovery from the anesthesia.

CASE 4. Mrs. H., age 45, blood pressure, 120, diastolic 80, radial pulse 80. No excitement; anesthesia and analgesia for 25 minutes for pulp removals.

CASE 5. Mrs. C., age 35, weight 130 lbs., blood pressure 110, diastolic 70, radial pulse 72. This patient preferred anesthesia to the least pain and was accustomed to it. The administration lasted 1 hour and 30 minutes. Erythrocytes decreased 400,000 per cm. The patient expressed a decided desire to rest after anesthesia, the rest terminating in sleep for 20 minutes After 2 hours rest and a light luncheon the erythrocytes showed an increase to 4,640,000. This patient had been anesthetized with nitrous oxid-oxygen for 1 hour the day previous.

CASE 6. Miss W., was of special interest owing to the fact that the nitrous oxid gave out and ethyl chlorid was substituted during the last 7 minutes of anesthesia. An increase of 36 per cent. in the erythrocytes was found immediately upon her return to consciousness. Ten days later nitrous oxid-oxygen was again administered and continued throughout the whole period of anesthesia and a decrease of 28 per cent. in

the erythrocytes was found on the patient's return to consciousness.

CASE 7. Miss P., 20, weight 120 lbs. The patient was kept under deep anesthesia or nearly so during the preparation of four cavities for filling. This case showed but very slight reduction in the number of red cells, a decrease of 0.7 per cent. being found immediately after her return to consciousness and of 0.9 per cent. one hour later. The leucocytes, however, showed an increase of 50 per cent. immediately after anesthesia, with a further increase to 69 per cent. one hour later.

CASE 8. Miss E., age 23, weight 110 lbs. Nitrous oxid-oxygen anesthesia for 35 minutes for extraction of teeth, and cocain locally during the removal of pulps.

STUDIES IN BLOOD CHANGES OF WILD AND TAME RATS UNDER NITROUS OXID-OXYGEN ANESTHESIA.

In making counts from both wild and tame rats the end of the tail was chosen for puncture before the administration, whenever practical, and the same technic was used at the close of anesthesia. When, however, it was impossible to obtain blood in this manner, it was taken directly from the coronary arteries of the heart. A discussion of some points of interest in the rats experimented upon will now be taken up while a detailed account of the blood changes has been summarized in the acompanying tables.

TABLE XII.

ERYTHROCYTES.

No. Case	Before N_2O-O	After N_2O-O	Percentage		Later	Exams	Percentage
			minus	plus	Time		minus plus
1. Mr. P.	3,688,000	3,424,000	7%				
2. Miss B.	4,488,000	3,800,000	15				
3. Miss R.	4,316,000	4,528,000		4%	.10	4,772,000	10%
4. Mrs. H.	4,640,000	3,360,000	22				
5. Mrs. C.	3,528,000	3,128,000	11		2.30	4,640,000	31
6. Miss W.	2,928,000	4,008,000		36	.40	3,524,000	20
6. Miss W.	4,248,000	3,036,000		28	.20	3,736,000	12
7. Miss P.	4,048,000	4,020,000	7		1.00	4,084,000	
8. Miss E.	4,276,000	4,720,000		14	2.00	4,484,000	48

LEUCOCYTES.

1. Mr. P.	7,500	8,500		13			
2. Miss B.	5,500	8,500		54			
3. Miss R.	6,500	9,500		46	.10	5,500	15
4. Mrs. H.	10,000	10,000					
5. Mrs. C.	6,500	6,500					
6. Miss W.	12,000	15,500		29	.40	9,500	25
6. Miss W.	12,000	5,500	54		.20	9,000	20
7. Miss P.	5,000	7,500		5	1.00	8,000	6
8. Miss E.	7,000	15,500		12	2.00	16,000	12

Erythrocytes showed an unusual increase of 440,000 after anesthesia. There was a gradual loss of red cells during the next two hours, at the end of which time the count was practically normal. The leucocytes showed a considerable increase in number during and after the administration of the anesthetic, with changes in the percentages of the varieties present. This case was rather difficult to manage throughout the operation as she never became subjective, but was continually resisting every movement of the operator. The patient showed great exhaustion for at least 2 hours after her return to consciousness, although she stated that she had no recollection of pain during the operation. These facts, combined with the use of cocain, may account for some of the unexpected changes found in the blood.

Rat 1. Tame, weight 60 grams. The animal was kept under a bell-jar of 4 litres capacity filled with nitrous oxid, for one minute, it was then removed and the inhaler placed directly over the nose. During the first four minutes there was spasmodic breathing, the heart beating at 134 beats a minute and the respiration being 92. At the end of four minutes, the rat stopped breathing for 30 seconds, life was restored by the removal of the anesthetic and careful manipulation of the chest. The heart beats rapidly increased up to

216 per minute and respiration reached 78. Blood was obtained from the tail before the gas was administered and from the heart at the close of anesthesia.

Rat 2. Tame, weight 65 grams. The heart beats were 136, but increased to 200 per minute during the five minutes the animal was under observation before any anesthetic was given. The animal showed great susceptibility to its environment. Death resulted two minutes after nitrous oxid was administered. Blood was obtained from the tail before anesthesia and from the heart afterward. The erythrocytes showed an increase of 25 per cent. after the administration of the anesthetic and the leucocytes showed a decrease of 11 per cent. There was also a marked increase in the small lymphocytes of 31.5 per cent.

Rat 3. Tame, weight 65 grams. Nitrous oxid-oxygen was administered for one-half hour, at the close of which time death resulted abruptly. The heart continued to beat for one minute and forty-five seconds after respiration had ceased. Blood was obtained from the tail before anesthesia, and from the heart after death. The erythrocytes showed an increase of 7 per cent., the leucocytes 29 per cent., during the administration of the anesthetic. A decrease of 5 per cent. in the small lymphocytes was also noted.

TABLE XIII.

HEMOGLOBIN.

No. Case	Before N_2O-O	After N_2O-O	Later Time	Examinations %
1. Mr. P.	77%	82%		
2. Miss B	77	73		
3. Miss R.	79	80		75%
4. Miss R.	89	93		
5. Mrs. H.	83	85	2.30	
6. Miss W.	75	75	.40	75
6. Miss W.	83	83	.20	83
7. Miss R.	82	82	1.00	82
8. Miss E.	85	85	2.00	85

ACTUAL QUANTITY

1. Mr. P.	10.55%	11.23%		
2. Miss B.	10.54	10.00		
3. Miss R.	10.82	10.96		10.68%
4. Mrs. H.	12.19	12.74		
5. Mrs. C.	11.78	11.64	2.30	
6. Miss W.	10.27	10.27	.40	10.27
6. Miss W.	11.27	11.27	.20	11.27
7. Miss R.	11.23	11.23	1.00	11.23
8. Miss E.	11.64	11.64	2.00	11.64

COLOR INDEX.

1. Mr. P	1.	1.		
2. Miss B.	0.8	0.9		
3. Miss R.	0.9	0.8		0.8
4. Mrs. H.	0.9	1.		
5. Mrs. C.	1.	1.		
6. Miss W.	1.	1.	.40	1.
6. Miss W.	0.9	1.	.20	1.
7. Miss R.	1.	1.	1.00	1.
8. Miss E.	1.	0.9	2.00	0.9

Rat 4. Wild, weight 3 lbs., 12 ozs. This rat was so large and vicious that it was anesthetized with ethyl chlorid six hours before the blood studies were made, so as to enable the operators to secure the animal in a safe position for work. Death resulted two minutes after induction of anesthesia with nitrous oxid-oxygen. The rat was found to be pregnant and tuberculosis of the lungs, liver and kidney presented an autopsy. Blood was obtained from the tail before and the coronary arteries after the administration of the gas. The erythrocytes showed an increase of 2 per cent., while the leucocytes remained practically unchanged.

Rat 6. Wild. Remained under the anesthetic 8 minutes before death occurred. Blood was obtained from the tail previous to anesthesia and from the heart afterward. Erythrocytes showed a decrease of 39 per cent., and the polynuclear neutrophiles a decrease of 25 per cent.

Rat 7. Wild. Died one minute and forty-five seconds after induction. Blood was obtained from the tail before anesthesia, from the heart afterward. Erythrocytes showed a decrease of 40 per cent., the leucocytes a decrease of 30 per cent. There was an increase in the lymphocytes of 5.9 per cent., and in the polynuclear neutrophiles of 20 per cent.

Rat 8. Wild. Died two minutes after induction.

Rat 9. Wild. Died three minutes after induction. The heart beat for nine minutes after cessation of respiration. Blood was obtained from the tail before anesthesia and from an artery lying just above the heart after the anesthetic had been removed. Erythrocytes showed a decrease of 19 per cent., the leucocytes a decrease of 17 per cent., and the small lymphocytes 7.3 per cent.

Rat 10. Wild. This rat escaped after the first specimen of blood had been withdrawn.

Rat 11. Wild. Died after being under the anesthetic for two minutes. No counts were obtainable after death.

Rats 12-13. Wild. These rats were killed by sudden trauma and their brains, long bones and organs were removed and prepared for histological examination.

Rat 14. Wild. Died after one minute of anesthesia. Blood obtained as usual. Erythrocytes showed a decrease of 27 per cent., leucocytes 20 per cent. decrease.

Rat 15. Wild. Death after thirty-one minutes of anesthesia. Blood obtained as usual. Erythrocytes increased 17 per cent. after removal of the anesthetic; leucocytes decreased 40 per cent. Blood was obtained from the heart immediately after death and a count of both red and white cells made. There were 1,040,000 fewer erythrocytes in the blood from the heart than in the blood from the tail. The number of leucocytes was the same in both specimen of blood.

Rat 16. Wild. Accidentally killed. Choked owing to the thick gloves worn by the operator. Owing to the difference which was found in the number of red cells in the blood from the tail and from the heart in Rat 15, a few more comparative studies were undertaken to determine, if possible, whether this was an occasional or the usual condition in animals under investigation. Accordingly three tame rats were obtained, approximately of the same weight, and a count was made of the red and white cells in the blood drawn from the tail immediately before anesthesia, and from the tail and heart immediately after death occurred. The differences in count obtained were within

the limit of possibilities for the blood stream in a living unit, and it is a practical fact that numercial counts are not the same at any two given periods of time. It must be noted, however, that in all instances a decrease in the number of red cells presented at the end of anesthesia.

Rats 17-18. Tame. These little animals were placed at the same time under a bell-jar, having a capacity of 4 litres, and nitrous oxid-oxygen was given by running the supply tube under the jar and pushing it up to a height of three inches within the jar. Air was excluded by placing towels around the lower part

TABLE XIV

No. Case	Ratio Between White and Red Cells: Before N_2O-O	Ratio Between White and Red Cells: After N_2O-O	Blood-Pressure: Systolic	Blood-Pressure: Diastolic	Coagulation Time: Before	Coagulation Time: After
1. Mr. P.	1.491	1.402	132mm.	Hg.85		
2. Miss B.	1.516	1.447	110	75	4min.	3min.
3. Miss R.	1.664	1.476	120	80		
4. Mrs. H.	1.464	1.336	120	80		
5. Mrs. C.	1.542	1.481	110	70	4min.	3min.
6. Miss W.	1.224	1.258				
6. Miss W.	1.354	1.550			3min.	2min.
8. Miss E.					3¾min.	2½

TABLE XV

No. Case	Polynuclear Neutrophiles: Before N_2O-O	Polynuclear Neutrophiles: After N_2O-O	Polynuclear Neutrophiles: Later Exams. Time	Polynuclear Neutrophiles: Later Exams. %	Small Lymphocytes: Before N_2O-O	Small Lymphocytes: After N_2O-O	Small Lymphocytes: Later Exams. Time	Small Lymphocytes: Later Exams. %
1. Mr. P.	94.6%	80. %			0.3%	13. %		
2. Miss B.	58.3	58.			32.5	32.6		
3. Miss R.	56.6	48.7			32.3	42.6		
4. Mrs. H.	66.	56.5			28.7	35.5		
5. Mrs. C.	57.	56.			36.	33.		
6. Miss W.	56.	63.3	.40	70. %	27.6	23.3	.40	21.6%
6. Miss W.	59.	54.	.20	55.	28.6	32.5	.20	34.4
7. Miss P.	63.3	63.7	1.00	68.	25.	15.	1.00	19.4
8. Miss E.	83.	73.1	2.00	88.1	7.2	19.	2.00	6.4
Transitional Forms					**Large Lymphocytes**			
1. Mr. P.						2.5%		
2. Miss B.	5. %	6.5%			3.5%	1.		
3. Miss R.	6.2	3.8			1.5	1.4		
4. Mrs. H.	1.1	5.5			1.8	1.3		
5. Mrs. C.	5.3	6.				3.		
6. Miss W.	10.7	6.	.40	6.3%	3.	2.3	.40	0.7%
6. Miss W.	5.	11.	.20	5.	4.6	1.5	.20	3.6
7. Miss P.	7.2	10.3	1.00	10.4	3.	8.	1.00	0.7
8. Miss E.	4.6	4.1	2.00	4.1	4.3	2.2	2.00	0.5
Eosinophiles					**Basophiles**			
1. Mr. P.	4.6%	4. %			0.5%	0.6%		
2. Miss B.		1.5			0.6	0.3		
3. Miss R.	3.4	2.7				0.6		
4. Mrs. H.	1.8	1.			0.6	0.2		
5. Mrs. C.	1.4	2.			0.2			
6. Miss W.	1.4	1.			1.2	1.	.40	0.3%
6. Miss W.	2.	1.			0.6		.20	0.3
7. Miss P.	1.2	2.			0.2	1.	1.00	1.
8. Miss E.	0.5	1.2			0.3	0.2	2.00	0.5

of the bell-jar. The nitrous oxid-oxygen was administered as follows:

Time	Nitrous oxid parts	Oxygen parts	
3.53	70	30	
3.56	75	25	
3.59	80	20	
4.02	85	15	
4.18	90	10	
4.36	100		Air and oxygen cut off.
4.38			Both rats collapsed.

Rat 17 was removed from the bell-jar and given a heavier dose of nitrous oxid; within three minutes death took place.

Rat 18 was removed from the bell-jar three minutes after partial collapse had occurred and was given the same amount of nitrous oxid that had been previously administered to Rat 17. Death took place in six minutes.

Rat 19. Tame. This rat was placed under a bell-jar and nitrous oxid-oxygen administered as in the experiments with Rats 17 and 18. A close inspection of the rat during the period of anesthesia resulted in obtaining some interesting data.

Time	N_2O	O	Reaction to the Anesthetic
9:45	50	50	Induction.
9:55	80	20	Normal.
10:00	85	15	Slight indications of anesthesia.
10:05	87	13	Cleaning face with paws.
10:07	88	12	Walked with hesitancy.
10:08	87	13	Dragged both hind legs.
10:10			Equilibrium lost; no movement on external stimulation.
10:15			Deep analgesia.
10:25	88	12	Dragged left side in effort to move body.
10:30			Slight amount of air admitted.
10:35			Breathing labored; no movement.
10:40			Slight amount of air admitted.
10:42	90	10	Breathing labored; no movement.
10:45	91	9	Rat expired.

The manner in which these little animals expired suggests some radical change in the respiratory centers. Respiration ceased about as quickly as under a small dose of nitrous oxid-oxygen, gradually increased, as it did under a large, overwhelming dose, with consequent sudden death. The heart continued to beat from three to thirteen minutes after the apparent cessation of respiration.

Rats are not very serviceable animals for study under anesthesia. Tame rats are rather too small and too susceptible to their environment to be anesthetized successfully, and wild rats have their powers of defense so highly developed that they fight to the bitter end; even in an apparently collapsed condition they will suddenly and most unexpectedly sink their teeth deeply into the glove of the operator.

TABLE XVI

POLYNUCLEAR NEUTROPHILES—SEGMENTS.

No Case	Before N_2O-O	After N_2O-O	Later Time	Exams. %	Before N_2O-O	After N_2O-O	Later Time	Exams. %
	1 segment				2 segments—connected.			
3. Miss R.	8.3%	21.4%			13.8%	7.3%		
6. Miss W.	11.3	7.	.40	9. %	9.2	12.	.40	6.7%
6. Miss W.	5.5	3.	.20	11.	2.1		.20	2.
7. Miss P.	11.	7.2	1.00	4.3	18.6	13.6	1.00	12.
8. Miss E.	10.	14.3	2.00		21.3	12.6		
	2 segments				3 segments			
3. Miss R.	49.7%	55.3%			25.8%	15.2%		
6. Miss W.	49.	53.5	.40	58.4%	27.	23.	.40	
6. Miss W.	48.2	44.	.20	52.	36.3	48.5	.20	21.4%
7. Miss P	41.	49.5	1.00	59.3	25.1	26.6	1.00	33.
8. Miss E.	46.	55.1			20.3	16.		22.5
	4 segments				4 segments			
3. Miss R.	2.3%	0.6%						
6. Miss W.	3.	4.5	.40	4.3	0.5%	83. %	.40	74.8%
6. Miss W.	6.2	4.	.20	2.	1.5	0.5		
7. Miss P.	3.3	2.5	1.00	1.4	1.	0.4	1.00	0.4
8. Miss E.	2.3	2.						

CONCLUSIONS.

The bibliographic review of this subject supplemented by experiments on human and animal subjects would indicate that hemoglobin is always reduced under anesthesia by chloroform, ether or nitrous oxid-oxygen. Hemoglobin is markedly reduced under ether, and the greatest reduction in pigment is at the end of 24 hours, after which there is a gradual return to normal in about 100 hours. Under nitrous oxid-oxygen anesthesia the reduction is not only slight, but the return to normal occurs in from 2 to 3 hours. Any

case presenting a color-index of hemoglobin below 60 per cent. should be considered a hazardous risk under ether anesthesia on account of the rapid reduction of hemoglobin during the first 20 minutes of etherization. Nitrous oxid-oxygen anesthesia or local analgesia is indicated in the presence of imperiling anemia when an operative procedure is imperative.

There is a polycythemia during ether anesthesia and an oligocythemia under nitrous oxid-oxygen. No marked change in the color-index is recorded in the original human or animal experiments reported in this paper. Hemolysis is observed under chloroform and ether, but no degenerated or crenated cells have been found on any of the slides made from the blood smears in the human or rat experiments herewith recorded.

Leucocytes have increased on an average under all anesthetic agents, although the records of Anders and Boston do not show this. The average increase in my personal experiments was 16 per cent. in human and 24 per cent. in the rat experiments. Chadbourne's cases give an average increase of 27 per cent.

The differential leucocyte counts have been made in too small a number of experiments to warrant the drawing of any definite conclusions. However, this seems to be a field worthy of close study, especially with regard to segmentation of the polynuclear neutrophiles, as has been indicated previously. Blood platlets are also an unexplored field in this subject.

The acid produciton of metabolism may be increased under anesthesia when deep cyanosis is permitted to occur or continue; but when a sufficient supply of oxygen is provided, this may be prevented. The hydrogen-ion is the

TABLE XVII.

No. Rat	Erythrocytes Before N_2O-O	Erythrocytes After N_2O-O	Erythrocytes Percentage Minus	Erythrocytes Percentage Plus	Leucocytes Before N_2O-O	Leucocytes After N_2O-O	Leucocytes Percentage Minus	Leucocytes Percentage Plus
1. Tame	6,024,000	5,772,000	41%		4,000	6,500		37%
2. Tame	6,552,000	4,864,000	25		8,500	7,500	11%	
3. Tame	6,872,000	7,388,000		7%	10,500	15,500		42
4. Wild	3,604,000	4,312,000		2	19,500	19,500		
6. Wild	7,084,000	3,632,000	39		3,800	7,000		84
7. Wild	6,096,000	7,424,000	40		5,000	3,500	30	
9. Wild	9,216,000	4,176,000	19		4,500	3,700	17	
14. Wild	5,776,000	6,096,000	27		5,000	4,000	20	
15. Wild	5,176,000	3,072,000		17	5,000	3,000	40	
17. Tame	5,328,000	3,144,000	42		3,800	1,700	55	
18. Tame	3,844,000		18		3,800	7,000		84
19. Tame	5,096,000	2,448,000	43		20,500	23,000		12

TABLE XVIII.

No. Rat	Lymphocytes Small Before N_2O-O	Lymphocytes Small After N_2O-O	Lymphocytes Large Before N_2O-O	Lymphocytes Large After N_2O-O	Transitional Forms Before N_2O-O	Transitional Forms After N_2O-O	Polynuclear Neutrophiles Before N_2O-O	Polynuclear Neutrophiles After N_2O-O	Eosinophiles Before N_2O-O	Eosinophiles After N_2O-O
1. Tame	73. %	55. %	8.2%	4. %	6.4%	13. %	12. %	28. %	0.3%	
2. Tame	34.	65.5	8.6	2.1	3.4	7.7	54.	22.5		2.1%
3. Tame	48.5	48.	8.5	2.8	1.2	1.9	42.8	47.3	0.2	
4. Wild	38.6	39.	8.	6.5	5.	2.3	48.2	52.2	0.5	
6. Wild	39.7	45.3	6.3	13.	2.	4.7	51.5	36.5	0.5	0.5
7. Wild	51.7	67.6	4.	5.2	4.5	5.2	39.2	19.	0.5	3.
9. Wild	76.7	69.4	4.3	10.6	0.5	4.6	17.3	14.2	1.2	1.

real constant in interpreting acidosis. In the color of the capillary blood the anesthetist has a valuable and delicate guage for determining the amount of oxygen necessary to prevent acid metabolic changes due to deep and imperiling or mild degress of long continued cyanosis. During cyanosis the hemoglobin of the blood gives up its oxygen to the tissues and this oxygen is not satisfactorily replaced, and consequent reductions in hemoglobin are noted.

While nitrous oxid-oxygen may well be considered the least harmful of anesthetic agents, nevertheless it is quite evident that certain definite blood changes present under its influence.

The averages obtained from the experiments on human subjects record decreases of 16 per cent. in the erythrocytes, with an increase of 16 per cent. in the white cells. The polynuclear neutrophiles showed an average decrease of 7 per cent., while there were average increases of 12 per cent. for small lymphocytes, 4 per cent. in the large lymphocytes and 16 per cent. in the transitional forms.

The percentage of hemoglobin also showed a tendency to decrease during anesthesia, while coagulation time of the blood was considerably shortened.

The experiments on rats corroborated the findings of the observations on the human subject. Thus the blood of rats showed an

TABLE XIX.

No. Rat	Ratio Between White and Red Cells		Hemoglobin		Actual Quantity		Color Index	
	Before N_2O-O	After N_2O-O	Before N_2O-O	After N_2O-O	Before N_2O-O	After N_2O-O	Before N_2O-O	After
1. Tame	1.1560	1.888	120%	120%	16.44%	16.44%	1.	1.
2. Tame	1.770	1.648	120	120	16.44	16.44	0.9	1.
4. Wild	1.184	1.189						
6. Wild	1.1864	1.616						
7. Wild	1.1219	1.1037						
9. Wild	1.2048	1.2006						
17. Tame	1.1402	1.1807						
18. Tame	1.1011	1.449						
19. Tame	1.248	1.106						

TABLE XX.

Red Blood Cells

No. Rat	Tail Before N_2O-O	Tail After N_2O-O	Percentage Minus	Percentage Plus	Heart Later	Percentage Minus	Percentage Plus
17. Tame	5,328,000	3,072,000	42%		3,062,000	42%	
18. Tame	3,844,000	3,144,000	18		3,062,000	23	
19. Tame	5,096,000	2,448,000	51		2,736,000	46	
		Average	43		Average	41	

White Blood Cells

17. Tame	3,800	1,700	55%		2,400	37%	
18. Tame	3,800	7,000		87%	11,500		202%
19. Tame	20,500	23,000		12	6,500	68	
		Average		25	Average		7

average decrease of 16 per cent. in erythrocytes immediately after the anesthetic was removed, and an increase of 24 per cent. in the leucocytes. The polynuclear neutrophiles gave an average decrease of 59 per cent., as did also the large lymphocytes, whereas an average increase of 16 per cent. was found in the small lymphocytes and 57 per cent. in the transitional forms.

Work, when accompanied by sweating, causes an increase in the red blood cells and in the percentage of hemoglobin. During anesthesia with nitrous oxid-oxygen there is usually marked perspiration, and a physical condition, resembling fatigue, which follows work, is evidenced by the patient. In contradistinction to the blood changes associated with work, however, anesthesia causes a rapid loss of red cells, this phenomenon occurring within a few minutes after the beginning of induction.

The question naturally arises: How are these red cells disposed of? Are they being rapidly destroyed by the spleen or are they being broken up into blood platlets?

Further question also arises as to the condition of the marrow in the long bones. Is there to be found in these factories of the red cells an increased proliferation of erythrocytes? Is the marrow crowded with neucleated cells and microcytes and is there a change in the other constituents of the red marrow?

A study of the brain in this respect has already been made. (See George W. Crile: Anesthesia, Anemia and Resucitation: herewith printed in the Year-Book).

Interest also centers around the changes in the heart, lungs, liver and kidneys, as influenced by the blood changes under anesthesia.

At present further studies in respect to these problems are being conducted by the author and his co-workers and the results will be reported at a future date. Larger animals will be used in these investigations and an especial study of blood platlets will be made.

In closing the author wishes to acknowledge his indebtedness to Dr. E. Q. St. John, through whose assistance and interested cooperation, abundant opportunities were afforded for the futherance of this work.

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RESEARCHES IN THE PERIPHERAL ORIGIN OF SHOCK • HISTORICAL REVIEW OF THEORIES • ORIGINAL INVESTIGATION OF THE PROBLEMS INVOLVED • THE STANDARD OF SHOCK • METHODS OF PRODUCTION • THE CONDITION OF THE VARIOUS TISSUES AND SYSTEMS IN SHOCK • NERVOUS, CIRCULATORY, RESPIRATORY AND VISCERAL ALTERATIONS • THE ROLE OF HEMORRHAGE AND INTRA-ABDOMINAL TRAUMA AS REAL CAUSATIVE FACTORS • SUMMARY OF RESULTS • CONCLUSIONS.

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DESPITE THE ENORMOUS amount of work which has been done on surgical shock, it has only been very recently that physiologists have begun to agree on the major principles in regard to its etiology. It is our purpose to bring together the most important of the experiments and conclusions upon which the present conception of shock is based.

THE DEFINITION OF SHOCK

The word *shock* is used in a very loose and vague way in medical literature. Some writers speak of *hemorrhagic shock*, *psychic shock*, or *toxemic shock*. This use of the term makes it synonymous with injury. A study of the clinical reports of the patients supposed to have suffered or died from shock shows how frequently this word covers our ignorance of what is really the cause of a patient's trouble, and also makes evident the necessity of excluding hysteria, cerebral injury, toxemia, concealed hemorrhage, the effect of heat or cold, and many other conditions before the diagnosis of shock is justifiable. The use of the word shock is comparable to that of the word rheumatism. The latter formerly included every disease of the joints, and many other diseases besides, but has been restricted gradually to very narrow limits.

As Meltzer,[1] Porter,[2] and others have emphasized, we have only a clinical definition of shock. No lesions of any organ or organs the presence of which will account for all the phenomena of shock have ever been conclusively demonstrated. The signs of shock are thus given by Meltzer: *"A state of general apathy, reduced sensibility, extreme motor weakness, great pallor, very rapid small pulse, thready soft arteries, irregular gasping respirations and subnormal temperature."* Meltzer insists that the presence of the circulatory phenomena is not absolutely necessary to the diagnosis. This definition is perhaps the best which can be given for this vague term, and with it we believe that most clinicians will be satisfied. It has the great merit of not invloving any more or less questionable theory of etiology. Such a condition may arise in the course of various diseases, or of surgical operations, or may result from accidents or intoxications. The word shock is often used where accidental or operative trauma has had nothing to do with producing the condition described. We have, however, for the sake of definiteness, limited our use of the word to conditions associated with trauma.

AN HISTORICAL REVIEW OF THE THEORIES OF SHOCK

The history of the development of present-day ideas of shock has been so carefully reviewed in recent years in several easily accessible articles (See 1, 3, 4, 5) that it is unnecessary for us to go into this phase of the subject in an exhaustive manner. We give the following brief historical review, not to evaluate or harmonize the various theories of shock

at present in vogue, but to show the unsettled condition of the whole subject, and how this state of affairs has come about.

In very early times it was observed that patients who had been injured might fall into a depressed lethargic state in which death might occur. Such cases were noted in which autopsy revealed no lesion adequate to account for death. The word *shock* was probably first used in the early part of the eighteenth century to describe an occasional effect of gunshot wounds, for it was believed that the impact of a bullet caused *a commotion of the elements of the nervous system* which accounted for the symptoms observed. From this period to the present almost every writer on surgical subjects has discussed shock. The ideas of older writers on shock were vague, though they foreshadowed nearly all the modern theories of this condition.

Thus Travers[6] (1826) states that *"shock is a species of functional concussion by which the influence of the brain over the organ of circulation is deranged or suspended."* And Savoy[7] (1860) writes that: *"death from shock results from sudden and violent impressions in some portions of the nervous system acting on the heart."* Thus writers have anticipated the modern theories of vasomotor paralysis and cardiac failure.

Delcasse[8] (1834) defined shock as *"an arrest of innervation without which all organs pass into insensibility."* This is the old way of stating Meltzer's inhibition theory.

Gross[9] (1872) poetically describes shock as *"a manifestation of a rude unhinging of the machinery of life."* Goltz[10] is (1872) usually regarded as having made the first noteworthy experimental observation bearing upon the etiology of shock in his well-known "Klopfversuch." This observation for a long time seemed to support the idea still held by many that vasomotor failure is the cause of shock. Although this theory, in a form more or less vague, had been held for a long time, Crile[11] in this country and Mummery[12] in England have been mainly responsible for formulating it definitely and for removing it from the realm of possibilities to that of supposedly demonstrated scientific fact. It has been most vigorously opposed by Porter.[13] The controversy between Crile and Porter is thus summarized by Meltzer:

"According to Crile the failure of blood pressure is the primary and sole cause of all the symptoms of shock, and this failure has as its cause solely the exhaustion of the vasomotor center. The cardiac and respiratory failures and their phenomena are only secondary consequences or subsidiary factors to the primary cause, the exhaustion of the vasomotor center . . . . "

The vasomotor studies of W. T. Porter alone and with his pupils led him to results and views entirely antagonistic to those brought forward by Crile. In the first place, in disagreement with Crile, he states that in his numerous experiments he failed to find an instance in which the stimulation of the afferent nerve caused a sufficient fall of blood pressure, except, of course, on stimulation of a depressor nerve. In his experiments crushing or electrical stimulation of the testis always gave a rise and not a fall of blood pressure. Continuous stimulation of the central ends of the sciatic, brachial or other afferent nerves for many hours gave uniformly the same rise of pressure as at the beginning. An analysis of 765 blood-pressure records from stimulation of the sciatic and brachial (and depressor) nerves of rabbits, cats and dogs brought out the result that the *percentage change in blood pressure, which is the true index of the condition of the vasomotor cells, increased as the blood pressure falls."* Even in experiments where all the clinical signs of shock were present, the blood pressure very low, the temperature subnormal, the heart beat weak and often irregular, and the irritability of the nervous system apparently much reduced, stimulation of the depressor nerve lowered the blood pressure by 45 per cent. All these data, says Porter, are wholly opposed to the hypothesis that exhaustion of the vasomotor center, brought on by over-stimulation, can be the cause of shock, but he is very emphatic in his assertion that the vasomotor cells in shock are neither exhausted, depressed nor inhibited. Porter contradicts Crile's facts and disagrees with his exhaustion theory; but apparently he also disagrees with Howell's view, that inhibition of the vasomotor and cardiac centers is at the bottom of the phenomena of shock.

The disturbance of pulse rate that is so often noted in shock has led some observers to look to a disturbance of heart action as a primary cause of shock. Thus Howell[14] thinks that one of the causes of shock is inhibition of the cardio-inhibitory center. Boise[15] states that the essential cause of shock is excessive sympathetic irritation manifested mainly by a tonic contraction of the heart and arteries. *"Shock is therefore due to cardiac spasm; an incomplete ventricular relaxation, mainly of the right side."* This reflex stimulation he supposes to pass through the accelerator nerves by way of the stellate ganglion.

Almost the exact antithesis to the vasomotor failure theory is the theory of Malcolm.[16] His view is that the arteries, more especially the peripheral arteries, are contracted during shock and that as a result of this the blood is "forced into the splanchnic area." This, he thinks, leads to important changes in the composition of the blood and tissues.

The idea that inhibition is a cause of shock is a very old one and is the basis of many theories. The terms vital depression, inhibition of innervation, inhibition of the vasomotor center, inhibition of the cardio-inhibitory center (Howell), all testify to the wide prevalence of this thought. Meltzer[1] has formulated the inhibition theory in the broadest and most satisfactory manner. He presents as evidence for his conclusions some observations upon the coecum of the rabbit. The movements of this organ can be observed in the intact animal through the abdominal wall. They cease when the skin of the abdomen is incised. He has shown that this is due to a definite inhibitory reflex. He thinks that perhaps other functions can be inhibited in a similar manner. He deserves special credit for emphasizing the fact that low blood pressure and an accelerated pulse rate are not always present in shock.

Leonard Hill[17] states that in his opinion shock is due to a depression of the sensory synapses, producing a decrease in tone of the central nervous system.

The most recent and at the same time the most radical departure from the older theories of shock is that of Henderson[18] who believes that shock may be caused by a loss of carbon dioxid by the tissues; the loss being brought about by excessive pulmonary ventilation or by exhalation of carbon dioxid from exposed viscera. He denies that vasomotor failure is present in shock and claims that the development of shock may be prevented by safeguarding the body from loss of carbon dioxid.

Various other possibilities have been suggested as a cause of shock. Among these might be mentioned the hypothesis that it is a derangement of the thermogenic mechanism;[19] that it is a condition of perverted metabolism due to trophic impulses;[3] that it is due to a pathological change in the chromaffin tissue;[20] or loss of adrenalin content,[21] that it is due to an inhibition of the muscle tone,[22]

ORIGINAL INVESTIGATION OF THE PROBLEM OF SHOCK.

A great amount of work upon special phenomena of shock has been done, for example, upon the state of arteries, the condition of the various vital centers, the specific gravity, and gaseous and cellular content of the blood. To much of this work we shall have occasion to refer later.

METHOD OF EXPERIMENTATION.

The experiments described in this article were performed upon animals which were under full surgical anesthesia. Ether was the anesthetic used. No animal was allowed to feel pain at any time, and all the animals were killed before they regained consciousness.

SCOPE OF THE PRESENT INVESTIGATION.

We wish to emphasize here at the beginning that the scope of the present experiments includes the phenomena which occur in the *anesthetized animal.* Our results, while strictly comparable to what may be observed on human patients during operation, do not apply to cases of so-called *pure shock* which may be met with under the conditions of ordinary life. Shock of this kind may be due to much more complex causes than the type we have studied.

ORIGINAL INVESTIGATION—THE STANDARD OF SHOCK.—We found it very difficult to determine when an animal had passed into a state of shock. In the protocols of some observers a markedly lowered pressure is taken as the sole indication of the presence of shock. Other

workers note, in addition to the blood pressure, the pulse and respiration. It can be demonstrated all too easily that low blood pressure, rapid pulse and irregular respiration may be produced by the action of the anesthetic alone. It seems to have been thought sufficient to state: "after reducing the animal to a state of shock, without giving either the method of its production or any criteria by which it is possible to judge whether the animal really was or was not in a condition of shock. This lack of definiteness in regard to these fundamental matters makes many of the most extensive researches on shock of somewhat questionable value.

We have regarded no animal as being in a condition of shock unless the following signs were present:

(1) *Loss of sensibility as shown by the lack of necessity of administering an anesthetic when the eye reflex was present.*

(2) *Pallor of the mucous membranes.*

(3) *Small, weak pulse.*

(4) *Irregular, rapid, shallow or gasping respiration.*

(5) *Markedly lowered blood pressure.*

The fundamental importance of these criteria merits a discussion of them. When all the above signs are present, and when there has been no hemorrhage, we believe that it will be generally admitted that shock in the full clinical sense of the term is present.

We were impressed by the fact that in many cases an animal might show all the signs given above except a markedly lowered blood pressure. Many times we observed dogs which presented pallor of mucous membranes and impaired respiration, and which required but little anesthetic for several hours, but in which the blood pressure was but 20 to 40 mm. lower than at the beginning of the experiment. In order, however, to make our results absolutely beyond criticism we always continued our manipulations until the blood pressure was only one-third to one-fourth its original level before we regarded the animal as in shock.

THE PRODUCTION OF SHOCK.—Our first endeavor was to find the quickest and most certain method of producing shock. We were exceedingly careful to avoid even the slightest hemorrhage. In a special series of twelve dogs experimented upon for this special purpose, and in a large number of others on which the observation was incidentally made, we attempted to produce shock by traumatization without opening the abdomen. Despite the most persevering efforts, we could reduce only two of these animals to a condition which was thought to be shock. In all others the blood pressure was just as high or only a few millimeters lower than at the begining, and just as much anesthetic had to be administered to keep the eye reflex inactive as is necessary in any experiment of the same length of time (3 to 5 hours).

It was also impossible to produce shock in an anesthetized animal by traumatization of the great nerve trunks. These results corroborate Porter's[13] conclusions. Long-continued stimulation, either electrical or mechanical, of large numbers of afferent fibers did not produce the condition. Intermittent stretching of a mixed nerve like the sciatic usually produced fluctuation in blood pressure, but intermittent and simultaneous stretching of both sciatics, both anterior crurals and both brachial plexuses for a period of four hours did not produce signs of shock. It is true that blood pressure, respiration and pulse were affected by these manipulations, but in no case were they markedly affected, provided, of course, that there was no hemorrhage. The blood pressure fluctuated slightly, rarely over 10 mm.; in some cases a slight fall occurred. The greatest fluctuation occurred under a light etherization. During deep anesthesia the most severe traumatization did not affect blood pressure, respiration or pulse.

In the two animals in which shock was thought to have developed, autopsy showed that very large concealed hemorrhages had occurred. These findings indicate that great care must be used to exclude hemorrhage before making a diagnosis of shock.

Our results in this special series of experiments and in many other experiments in which we have had occasion to observe the effects of trauma upon the anesthetized animal are so consistent and invariable that we do not hesitate to state that it is impossible to reduce a dog to a state of shock in 4 to 5 hours by traumatization alone, without opening the abdomen, without inducing hemorrhage or without trauma to the medullary centers. These

results corroborate the findings of Hill[23] and also of Janeway and Ewing.[24]

THE PRODUCTION OF SHOCK BY THE USE OF EXCESSIVE HEAT OR COLD.—Heat: Investigators who have used heat to produce shock have endeavored to stimulate as many sensory nerve endings as possible. There are, moreover, many factors other than the stimulation of the sensory fibers involved in such experiments. Perhaps the most important of these is the increase in the temperature of the animal. Since the dog eliminates heat chiefly by way of the lungs, its respiration is greatly increased in rate and depth. That this hypernoea is due mainly to the increased temperature may readily be shown by applying cold to the parts of the animal which are not subjected to the heat. If this be done, the hypernoea will not occur. Furthermore, we shall cite evidence to show that heating the blood causes important changes in the various tissues of the body.

We have found that heat applied to the feet or large body surfaces of the etherized dog does not produce any permanent effect upon its blood pressure, although slight fluctuation of the same may occur during application. In order to control the conditions of the experiment better we devised a method of heating only the blood of the animal. This was accomplished in three different ways:

First: Both carotid arteries for as long a distance as possible were carefully freed from the neighboring structures which were protected from heat by gauze saturated with salt solution. Warm water was then circulated through the coil which encircled each carotid.

Second: The hind leg of the animal was completely severed from its body except for the femur and femoral vessels. These vessels were dissected free for some distance and gauze saturated with salt solution at 60° C. was placed around them.

Third: By injecting hot water into the rectum.

Heat applied in any of these ways will reduce a dog in from two to three hours to a condition in which all the signs of shock are present. If light anesthesia be used hyperpnoea will develop, but if the dog be deeply etherized the pulmonary ventilation is decreased. We have observed no effect of the breathing in either case on the time at which shock developed. In the experiment on the dog with the partially severed leg this limb at autopsy was found to be swollen to several times its normal size. On incising it clear fluid poured freely from the cuts. In all the animals the blood at autopsy was found to be dark and thick and all the veins, both splanchic and peripheral, were dilated.

The condition produced in these experiments fulfilled all the requirements of the clinical definition of shock. Death seemed to result from primary cardiac failure. We can state most emphatically that the condition did not result from traumatic stimuli, or loss of carbon dioxid, but was wholly due to overheating of the blood. We positively demonstrated that the vasomotor center was active, because it constantly responded to the tests which we shall discuss later.

The effect of excessive cold was observed upon an animal which was subjected to a continuous real injection of ice water. In an hour and a half the animal was reduced to a condition resembling shock. The only noticeable difference between the condition of the animal in this experiment and that of those which had been subjected to heat was the character of the pulse. The rate of the heart beat was greatly decreased and the amplitude of the beats increased. Section of the vagi only slightly modified the cardiac action. The animal died from primary cardiac failure.

THE PRODUCTION OF SHOCK BY FORCED VENTILATION OF THE LUNGS.—We attempted to produce shock by Henderson's[18] method of forced lung ventilation. In a limited number of experiments of this character we were able to produce the condition in only one case. Our trouble was probably the same as Henderson records in regard to his first experiments—an inefficient pump. However, it seemed that the artificial ventilation was certainly as great as the animals themselves would be able to produce. Our results were therefore negative.

THE PRODUCTION OF SHOCK BY OPENING THE ABDOMEN AND EXPOSING THE VISCERA.—Our next method was to open the abdomen and expose and traumatize the viscera. This in every instance produced shock. Sometimes the condition came on quite rapidly; in other instances the process was delayed. Upon opening the

abdomen the blood pressure usually fell, due to lowered intra-abdominal pressure. While the viscera were being exposed the blood pressure showed marked fluctuations, due to the mechanical manipulations. If the intestines were squeezed the pressure might temporarily become greater than normal, because of the better filling of the right side of the heart. But gradually blood pressure fell and usually within an hour or two shock was present. In many cases it was not necessary to administer ether after the abdomen was opened, even when the experiment extended over a period of several hours.

In reviewing the protocols of various observers it is interesting to note their use of visceral traumatization to produce shock. It is surprising how few experiments are on record in which, if the method of producing shock is stated at all, this was not the means employed. The observer may begin an experiment by crushing a foot or burning a part, and may obtain some fluctation in blood pressure by such means, but sooner or later, as if discouraged by the progress made, he invariably adds, "and the intestines were manipulated." The protocols are few which do not record directly or indirectly a complicating hemorrhage or a section of the abdomen.

In all our experiments, unless otherwise stated, shock was produced by exposing and traumatizing the abdominal viscera of an etherized animal. The condition was never called shock unless the clinical signs as previously stated were present, except in special experiments, e. g., in the use of curare, or section of the cord, which made it impossible to note some of the signs.

THE CONDITION OF VARIOUS TISSUES AND SYSTEMS IN SHOCK.

An endeavor has been made to study individually each system which might be affected in shock, the attempt being to determine what part it played in the production of shock, and how it was affected by the resulting condition.

THE VASOMOTOR MECHANISM IN SHOCK.—The Vasomotor Center: Our work corroborates Porter's[13] conclusions in regard to the condition of the vasomotor center in shock. Stimulation of mixed nerves produced a marked rise of blood pressure, even in extreme degrees of shock, and stimulation of the depressor nerve produced a comparable fall in the same condition. We were able to corroborate Seelig and Lyon's[25] results in regard to the effect upon the blood pressure of stimulating the central end of the vagus. In every case this yielded a rise of blood pressure in shock. In some instances the rise was actually greater in the shocked animal than in the normal one.

The reaction of the center to the concentrated hydrogen ion content of the blood is as marked after the production of shock as before. The production of a wide pneumothorax in a shocked animal gives a blood pressure tracing not influenced by the respiratory movements. Under these conditions an asphyxial rise in the blood pressure takes place. In some cases the pressure of an animal in marked shock was more than doubled; in other instances but a moderate, and rarely but a slight rise occurred. The same result was obtained if the animal were made to inhale high percentages of carbon dioxid. The injection of lactic acid does not produce a constant result even in the normal animal. However, we have records which show a marked increase in blood pressure in the shocked animal produced by this supposedly normal chemical stimulant. An increase of intracranial pressure produced the same relative increase of blood pressure in the shocked animal as in the normal one.

THE CONDITION OF THE ARTERIES IN SHOCK.—The Peripheral Arteries: The pallor which occurs in shock might be due to one of two causes: (1) The constriction of the peripheral vessels, which prevents a flow of blood to the skin; or (2) to a dilatation of the splanchnic vessels, which causes the blood to be drained out of the skin. Seeling and Lyon[26] have recently investigated the condition of the peripheral arteries in shock and have concluded that these vessels are constricted. Bartlett,[27] who has investigated the same question, reaches an exactly contrary conclusion.

Neither of the methods used by these investigators gave conclusive results in our hands. However, Morrison and Hooker,[28] using practically the same method as Bartlett, obtained exactly the opposite result. During the production of shock, peripheral venous pressure,

as taken from the femoral vein, decreases. This is usually very marked and may take place before blood pressure has greatly decreased. If the sciatic is cut in the shocked animal there is an immediate and decided increase in the pressure of the femoral vein. This is evidence that the arteries of the limb are constricted during the production of shock and that there is considerable vasomotor tone, even when the blood pressure is very low. These results have been confined by other methods of experimentation by Morrison and Hooker,[28] and also by Janeway and Jackson.[29]

The tongue of the dog is an organ which is liberally supplied with vasomotor fibers. Fortunately these run in separate nerve trunks. The major part of the dilators pass through the lingual nerve[30] while the constrictors are carried in the hypoglossus. This furnishes an ideal arrangement for the study of this particular phenomenon. If one hypoglossal nerve is stimulated in a curarized dog, the tongue becomes slightly paler on the side innervated by this nerve; if the lingual nerve is stimulated, the tongue becomes very red and the veins stand out very prominently upon the corresponding side. If the animal is reduced to shock the phenomenon, upon stimulating the lingual, is even more marked. The reddened muscles and bulging veins of the corresponding side contrast strikingly with the pallor of the opposite side of the tongue and the mucous membrane of the oral cavity. The vessels of the tongue are evidently in tone which is decreased by the stimulation of the dilator fibers. This tone might be due to vaso-constrictor impulses from the vasomotor center or the arterial muscles themselves. That at least a part of this tone is due to the former cause is proved by the gradual but quite noticeable dilatation which occurs after section of the hypoglossal nerve which contains the vaso-constrictor fibers. In animals which normally have enlarged vessels of the tongue this result can be better observed if a slight asphyxia is produced in the shocked animal.' Tracings of the volume of the tongue of a dog in shock show that it is decidedly increased upon stimulation of the lingual nerves. This experiment proves that the arteries of the tongue are still subject to considerable vasoconstriction in shock.

A large number of the vasoconstrictor fibers of the rabbit's ear run in the cervical sympathetic nerve[31] which forms a separate trunk in that animal. The blood vessels of the ear of the albino rabbit show vasomotor changes quite distinctly. As shock develops, these blood vessels become constricted until they are small, more or less faint, lines. That this decrease in caliber is not a passive condition is shown by the fact that lowering of the ear below the level of the splanchnic area does not produce a congestion of these vessels, while section of the cervical sympathetic nerve produces a noticeable dilatation of them. They are, therefore, under vasomotor tone in shock. These results corroborate those of Seelig and Joseph.[32]

The unpigmented paw of a kitten or puppy is well suited for the study of vascular changes in the limbs. The vasomotor fibers of the paw run in the sciatic nerve.[33] If the sciatic on one side is cut in the normal animal the corresponding paw assumes a brighter tint than its fellow. In the beginning of shock the difference becomes more marked, because the paw with the intact nerve becomes paler. It is only when the blood pressure is very low in marked shock that the paws look alike. Even then a difference can be observed by lowering both paws below the level of the splanchnic area, when the paw with the intact nerve becomes paler. If the sciatic of the intact leg be now severed a faint but distinct flush appears on this paw. This experiment shows that the blood vessels of the paw are under vasomotor tone in shock.

THE UNTRAUMATIZED VISCERIAL ARTERIES IN SHOCK.—The arteries of the kidneys were taken as the most accessible of the untraumatized visceral arteries to study. The vasomotor changes were recorded by means of an oncometer. This can be applied through a lumbar incision without entering the abdominal cavity and without disturbing blood pressure. Tracings of the volume of the kidneys were taken before, during and after the production of shock.

During the production of shock there was usually an immediate kidney shrinkage, although this did not invariably occur, for at times an initial expansion occurred, while in other instances the volume of the kidney pass-

ively followed the changes in the general blood pressure.

Roy and Bradford[34] have shown that stimulation of the central end of the sciatic nerve produces a decrease in kidney volume, while it increases the general blood pressure. Our results show that when the blood pressure is very high in the normal animal, stimulation of the sciatic nerve does not always produce a shrinkage of the kidney. A slight expansion may occur, but this increase in kidney volume is always so small as to show that some vasoconstriction is occurring, although not quite enough to offset the rise in general blood pressure.

Stimulation of the sciatic nerve in moderate degrees of shock *always* produces a marked decrease in kidney volume, although the rise in general blood pressure might be as great as in the normal animal. In some cases this decrease in kidney volume following stimulation of the sciatic could be obtained with a blood pressure of only 20 mm. Additional evidence of the vasoconstrictor tone of the renal vessels was secured by recording the increase in volume of the kidney following cauterization of the renal vessels with carbolic acid, which destroys the vasoconstrictor fibers.

It is evident from these experiments that the tone of the vasoconstrictor mechanism of the kidney is increased in a moderate degree of shock, and that is not entirely absent even when the blood pressure is very low.

THE CHARACTER AND FLOW OF THE LYMPH IN SHOCK.—This was investigated by observing the rate of flow from the thoracic duct. A canula was inserted into the duct extrapleurally without producing any disturbance in blood pressure or respiration. The rate of flow was determined by counting the drops or accurately measuring the amount of flow per unit of time. Care was taken during the reading to exclude the effect of irregular respiration or manipulation of the intestines. A normal rate was always determined before shock was produced. The following results were obtained: At the onset of shock the lymph flow through the thoracic duct was slightly increased. As shock developed it might decrease slightly below normal. In character the lymph changed from a color more or less milky to a pale reddish color. Microscopic examination showed many red cells present. The coagulation time was markedly decreased, so much, in fact, that toward the end of an experiment it was almost impossible to maintain a flow from the canula. At this time the lymph resembled an exudate.

THE CARDIO-INHIBITORY CENTER IN SHOCK.—This center is thought by some investigators to be inhibited in shock, while others claim that it loses tone. The following facts throw light upon this point:

An animal which has had the vagi cut does not seem to develop shock any more quickly than one in which they are intact.

It is well known that if one vagus is severed while the other is left intact and the central end of the divided one stimulated, a rise in blood pressure occurs. However, by carefully graduating the current in some animals a reflex inhibition of the heart can be procured. In each dog in which it was possible to obtain this reflex it remained positive, even in the most extreme degrees of shock. That this inhibition of the heart was a definite reflex, involving the inhibitory center, was shown by section of the intact vagus in the deeply shocked animal; after this it could not be again obtained.

In the normal adrenalin curve, after the initial rise in blood pressure, inhibitory beats occur which have been proved to be due chiefly to a reflex involving the inhibitory center, although increased filling of the heart may be a factor. In the tracing obtained by the injection of adrenalin in the shocked animal the same characteristic beats occur, after blood pressure has slightly increased. We observed their disappearance in shock after section of the vagi and an increase of blood pressure to six times the height present before the drug was injected.

An increase in intracranial pressure produces characteristic inhibitory beats of the heart, due in all probability to bulbar anemia. These occur when the intracranial pressure is increased in the shocked animal, and cease when the vagi are cut. The blood pressure then increases enormously, for the vasomotor center also reacts to the increased intracranial pressure.

These experiments would seem to prove con-

clusively that the cardiac inhibitory mechanism is intact, even in the deeply shocked animal.

THE HEART IN SHOCK.—In all the experiments in which the animal was allowed to die from uncomplicated shock the heart was beating, although sometimes quite feebly, when respiration had ceased and blood pressure was practically zero. In many cases, upon opening the thorax when all signs of life had disappeared, the heart was observed to be contracting still. In the production of shock the pulse usually, but not invariably, increased in rate. The individual beats always became weaker, as measured by palpation and the manometric tracing, but the cardiac function remained until the very last.

Seelig and Lyon[26] have shown that typical shock can be produced after evulsion of the stellate ganglion. This certainly removes almost entirely the possibility of the heart being affected through the sympathetic system.

That the heart is capable of performing its function efficiently in shock, if only enough blood is returned to it, was pointed out by Hill.[35] He increased the venous return to the heart by visceral compression and noted that the heart was able to handle the increased amount of blood effectually. We have been able to corroborate Hill's results.

A more severe test of efficiency of the heart in shock is afforded by the injection of large doses of adrenalin in the shocked animal after section of the vagi. This produces an enormous rise of blood pressure, often increasing the pressure to a level six times higher than that in shock. In every instance in which this was done the heart was able to pump against the enormous pressure effectually and in no instance was there an indication of cardiac failure. A similar test was made by increasing the intracranial pressure of a shocked animal in which the vagi had been cut. The vasomotor center was stimulated and the blood pressure increased enormously, but although this was maintained for several minutes, the heart remained competent to perform its function.

In view of these facts it is impossible to believe that the heart is the primary factor in the production of shock. These experiments prove that the heart is as efficient a pump in shock as in any other condition in which it has been subjected to a poor blood supply during a long period.

THE RESPIRATORY MECHANISM IN SHOCK.—As shock develops, respiration becomes more shallow and may increase in rate, but quite often decreases. The most characteristic respiratory phenomenon of shock is the intermittent gasping type of respiration. All our tracings obtained from animals which died of uncomplicated shock show that the respiration failed before the circulation. However, the respiratory center of a shocked animal responds quite actively to inhalation of carbon dioxid and to the injection of lactic acid. Stimulation of the vagus produces the usual inhibition of respiration in the shocked animal.

These facts show that the respiratory mechanism is not primarily at fault in the production of shock, but that it is probably the most seriously damaged and the most easily injured of the medullary centers by the resulting condition.

THE STUDY OF THE MESENTERIC CIRCULATION IN SHOCK.—In many experiments a microscopical study of the circulation of the mesentary and omentum was made. The phenomena observed were those described by the pathologists in the classical descriptions of acute inflammation. These are: Dilatation of arteries and veins; congestion and slowing of the venous flow, which later results in a more or less noticeable stasis; margination and later emigration of the leucocytes; late in the condition rupture of many of the small vessels and escape of cellular elements into the tissue spaces or to the surface.

Histological sections of the omentum, mesentery and intestines of the normal and shocked animal were made and compared. These showed all the above phenomena in a static form and emphasized many of the facts which will be discussed later.

THE CONDITION OF THE BLOOD IN SHOCK.—Specific Gravity: There has been considerable controversy in regard to the specific gravity of the blood in shock. The preponderence of the evidence is in favor of an increase of specific gravity in this condition. We observed that if the blood were taken from the peripheral vessels it showed by a slight increase in its specific gravity, but if taken from

the splanchnic vessels it showed a marked increase.

THE BLOOD CORPUSCLES IN SHOCK.—Crile[36] in a series of four experiments upon shocked dogs and dogs suffering from hemorrhages, comes to the following conclusions: In shock the red cells are increased while the white cells are decreased; in hemorrhage red cells are decreased while white cells are increased.

The condition of the blood in hemorrhage need not be discussed or investigated here, especially as this has been done so completely by many observers. In general our results corroborate those of Crile.

zation for a period of five minutes would lower blood pressure considerably, but if the traumatization were now stopped the pressure would soon return almost to normal. However, if the traumatization were continued for a much longer time the animal would develop signs of shock. That this was not due to an exhala-

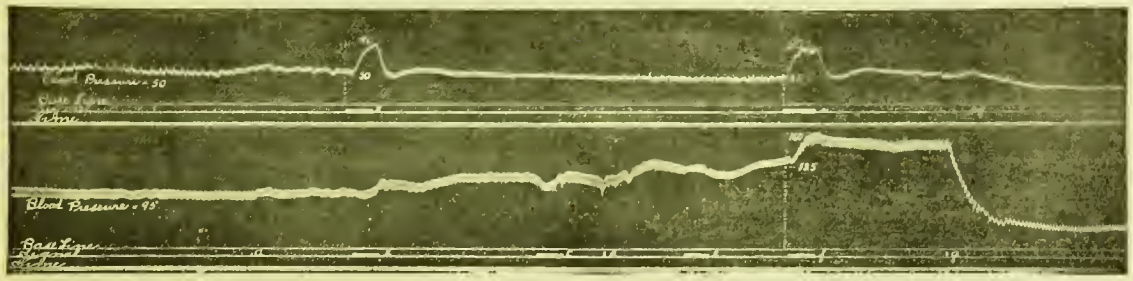

Figure 1. Normal blood pressure 95. Right and left vagus sectioned at *a* and *b* respectively. At *b*, *c*, *c*, and *h*, central end of right vagus stimulated. Central end of left vagus stimulated at *f* and *i*. At *g* the animal was bled 37 per cent. of its blood. At *j* it was bled to death. Note the reaction of the vasomotor center after hemorrhage.

tion of carbon dioxid was proved by passing a stream of high percentage of this gas directly into the abdominal cavity. If the gas were admitted slowly so as not to increase the intra-abdominal pressure it did not delay the onset of shock.

PRODUCTION OF SHOCK AFTER SECTION OF

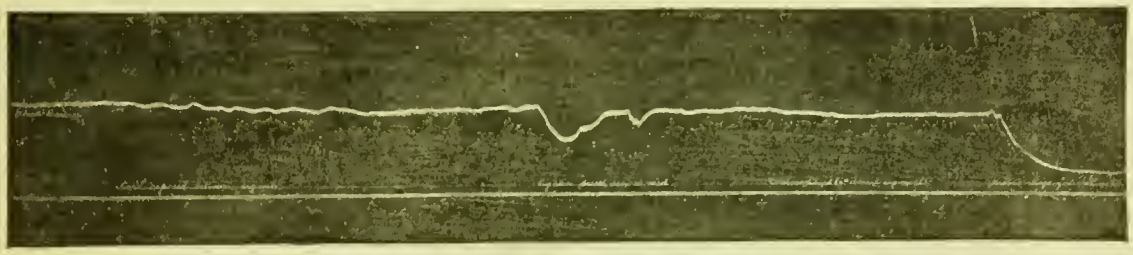

Figure 2. Normal blood pressure 145. Marked fall in pressure when ligature was passed around cord. After section of sixth cervical segment blood pressure remained at 100; 65 per cent. of blood was secured from femoral artery and 12 from the heart.

METHODS OF PRODUCING SHOCK.

THE PRODUCTION OF SHOCK BY INTRA-ABDOMINAL TRAUMATIZATION WITHOUT FREE EXPOSURE OF THE VISCERA TO THE AIR.—In some experiments an incision into the abdomen just large enough to admit the hand was made. Through this a gloved hand was passed and the abdominal wall clamped snugly around the wrist. Intra-abdominal traumati-

THE CORD.—Section of the cord in an animal in the horizontal position in the lower cervical or upper dorsal region produces an enormous fall of blood pressure, due to section of the vasoconstrictor fibers. That such an animal is not in a condition of surgical shock can be shown by withdrawing the anesthetic, when the animal will regain consciousness and respond to stimuli applied around the head. Upon opening the abdomen of an animal in this

condition the vessels of the splanchnic area are seen to be dilated and the viscera congested. But the exposure of the viscera produces a marked and immediate increase in the congestion in the same manner as in an animal which has not been subjected to section of the cord. The fall of blood pressure following section of the cord is not any greater than the decrease which follows soon after section of the abdomen and exposure of the viscera. Evidently typical shock can be produced after section of the cord.

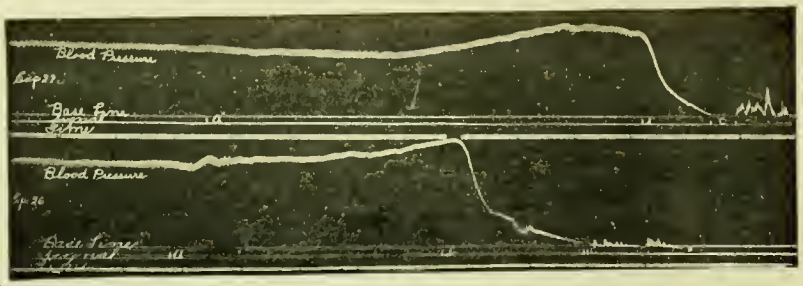

Figure 3. Normal blood pressure 128. Began to push ether at *a*. Respiration failed at *b*. Femoral artery was opened and artificial respiration started at *c*. Obtained 48 per cent. of blood from artery, 15 from heart. Almost similar record below

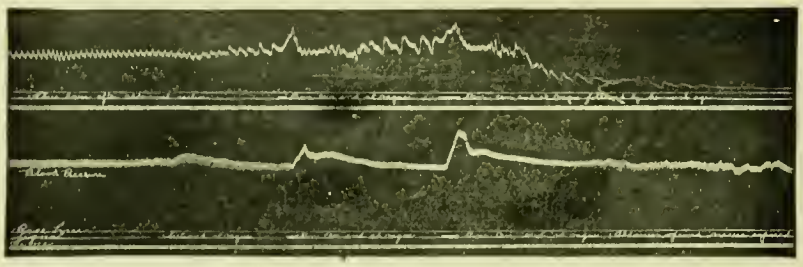

Figure 4. Normal blood pressure 122. After exposing viscera for 3 hours it had decreased to 70. Reaction of vasomotor center practically normal. Obtained 31 per cent. of blood from artery and 11 from heart.

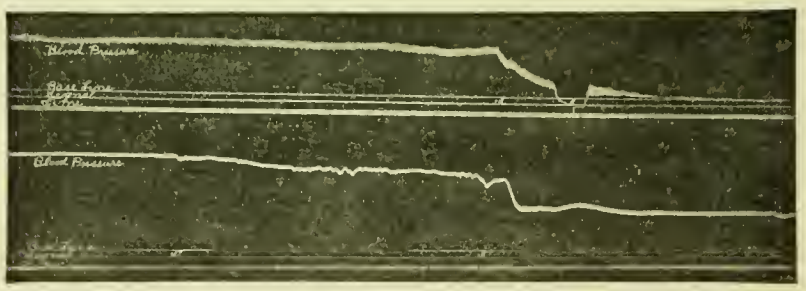

Figure 5. Normal blood pressure 145. Cervical cord exposed between *a* and *b*. Fall in blood pressure due to passing ligature around cord. Cord sectioned at sixth cervical segment at *c*. Blood pressure fell to 60, but after 2.30 increased to 75, when the femoral artery was severed, *d*. Obtained 52 per cent. of blood from artery and 11 from heart.

THE EFFECT OF HEMORRHAGE UPON THE PRODUCTION OF SHOCK.—During the course of some experiments accidental hemorrhage occurred. It was noted that shock developed

very quickly in these cases. This observation agrees with the reports of a large number of clinicians. In order to study this condition more completely a series of experiments was performed in which the animals were subjected to varying degrees of arterial or venous hemorrhage and the same tests applied as in the experiments upon the shocked animal.

The most noticeable effect of a slight hemorrhage upon an anesthetized animal is the resulting depression of sensation. A dog of 5 kilos weight could be subjected to a slow venous hemorrhage of 50 to 75 c.cm. without producing a fall in blood pressure of over 15 mm. But the loss of sensibility was such that in most cases only a very little, if any, anesthetic was necessary, even in long-continued experi-

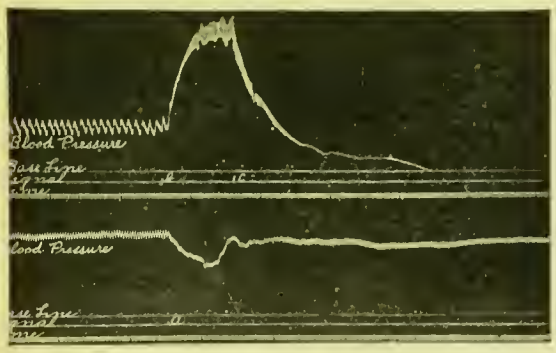

Figure 6. Normal blood pressure 110. Abdomen opened at *a*. When animal was in shock with blood pressure at 50, 2 ccm. of adrenalin was injected, *b*. Femoral artery opened at *c*. Obtained 38 per cent. of blood from artery and 8 from heart.

ments. If the bleeding were done from an artery of large size, as the femoral, blood pressure fell quickly during the hemorrhage, but if the loss of blood were slight, vasomotor compensation would restore the pressure almost to normal. As the amount of blood lost was increased the power of vasomotor compensations decreased until blood pressure remained very low. Furthermore, we found that the animals which had been bled responded to the same tests for the activity of the various centers in the same manner as the animals which had been reduced to shock. The condition of an animal after hemorrhage could not be differentiated from the condition of shock.

THE AMOUNT OF CIRCULATING FLUID IN SHOCK.—Lyons and Swarts[37] have found a decrease in the amount of blood in all organs of the shocked animal. Our problem was to determine whether there is in shock an actual loss of circulating fluid and, if so, what factors are mainly responsible for this loss.

The amount of blood that can be obtained from a large arterial trunk,— as the femoral, —is the measure of efficient blood; it is the amount which can be returned to the heart and lungs, and after aeration, be pumped out to feed the tissues. The blood which can be secured from the venous side of the circulatory system,—as from the right auricle,—is the amount that is freely movable but was not returned to the heart. Their sum is the amount of mobile blood in the body. This sum substracted from the total amount of blood gives the quantity of immobilized blood, the fixed quantity in the tissues. So far as the immediate circulatory needs of the organism are concerned, this latter amount of blood is useless.

In our experiments the total amount of blood was estimated in its relation to the body weight. The percentage used was 7.7 per cent, or one-thirteenth of the total weight of the animal. This standard is open to a certain degree of error, particularly since it was impossible to obtain enough dogs of approximately the same size and breed. However, this source of error was reduced to a minimum by using in each series the same type of animals in the same physical condition, as the study is of comparative conditions, the variation does not materially affect averages.

The general technic was uniform in all the experiments. The animal, which had been fasted for eighteen hours, was etherized and carefully weighed. The anesthesia was maintained by the auto-intratracheal method.[38] Blood pressure was taken from the right carotid artery. A cannula was placed in the right femoral artery. After performing the experimental procedure such as producing shock, or sectioning the spinal cord, the femoral artery was opened and all the blood that could be secured was obtained. The thorax was then opened, the pericardium stripped over the heart and, turning the animal on its side in a slight Trendelenburg position, the right auricle and, later, the cava were opened, allowing the blood to flow into a wide-mouthed receiver.

The exact weight of the separate specimens was recorded.

The observations fall into four different groups: (1) In the first series normal dogs were used as controls to determine how much blood can be obtained by the method described; (2) in the second series the cervical cord was cut before bleeding; (3) in the third series the animals were practically killed with ether and the bleeding was done after the institution of artificial respiration; (4) in the fourth series the animals were shocked by exposure of the

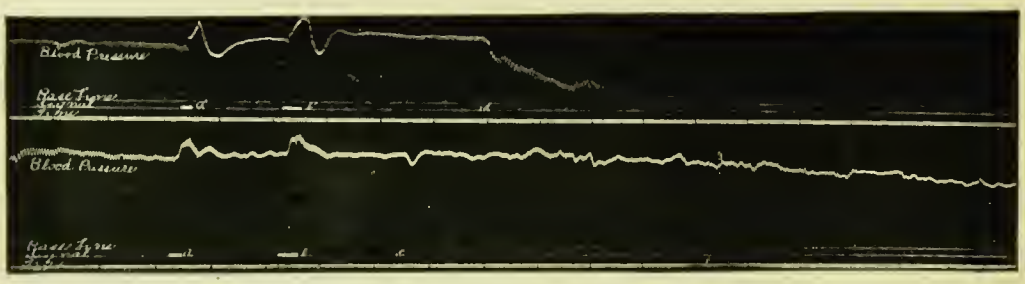

Figure 7. Normal blood pressure 150. Signals *a* and *b*, and a and b, mark point of stimulation of central end of right vagus Abdomen opened at *c*. After exposure of viscera, blood pressure fell to 90 and animal did not exhibit all the signs of shock. Note reaction of vasomotor center; 38 per cent. of blood secured from artery and 9 from heart.

Figure 8. Normal blood pressure 130. Between *a* and *b*, 26 per cent. of the animal's blood was removed by slow hemorrhage from the femoral vein. Blood pressure fell to 110. Between *c* and *d*, 10 per cent. more was removed. Between *d* and *e*, 7 per cent. bled from the femoral artery. At *f* bled to death from femoral artery.

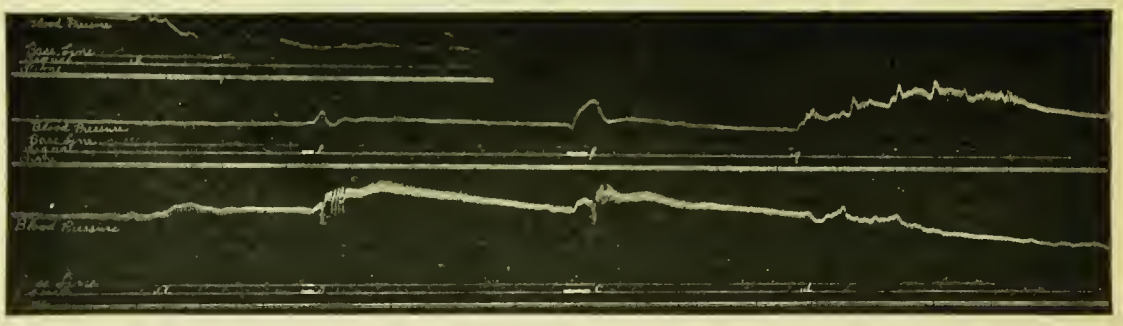

Figure 9. Normal blood pressure 100. Right vagus cut at *a*. Central end stimulated at *b* and *c*. Abdomen opened at *d*. Blood pressure decreased to 30. Animal in deep shock; vagus again stimulated at *e* and *f*. Note reaction of vasomotor center. At *g* injected 240 gms. of citrated blood (equal to about 35 per cent. of the animals blood). Blood pressure at first increased, but in 30 minutes was only 64. Bled at *h*, obtaining 385 gms. from the artery and 63 gms. from heart.

abdominal viscera. Several experiments devised to emphasize certain points are also reported.

The data from the experiments herewith reported may be summarized as follows:

(1) In a normal dog 66 per cent. of the blood can be obtained from the femoral artery and 10 per cent. from the heart, making a total of 76 per cent. which can be secured, leaving 24 per cent. in the tissues.

(2) In an animal in which the cervical cord is sectioned, producing medullary vasomotor paralysis, 54 per cent. of the blood can be obtained from the femoral artery and 12 per cent. from the heart, a total of 66 per cent., cent., leaving 41 per cent. in the tissues.

(3) In an animal in which blood pressure is depressed practically to zero by an overdose of ether, 46 per cent. of the blood can be obtained from the femoral artery and 13 per cent. from the heart, making a total of 59 per cent. leaving 41 per cent. in the tissues.

(4) In an animal in which the viscera have been exposed until the clinical signs of shock are present but in which the vasomotor reflexes are as active or even more so than in the normal condition, only 28 per cent. of the blood can be obtained from the femoral artery and 11 per cent. from the heart, making a total of 39 per cent., leaving 61 per cent. in the tissues.

(5) In the special experiments it was determined: (a) that a free hemorrhage of the amount found to be lost in shock produced all the clinical signs of shock; (b) that increase of peripheral resistance in the shocked animal by the injection of adrenalin did not materially increase the amount of obtainable blood.

SUMMARY AND CONCLUSIONS.

The data from our own experiments and those of other investigators justify the following conclusions:

(1) We have been unable to reduce the anesthetized animal to a state of shock by any degree of sensory stimulation, provided all hemorrhage is prevented and the abdomen is not opened.

(2) We have been unable to show that acapnia is a primary factor in the production of shock.

(3) Shock is not due to disturbance of the respiration, but the respiratory center is more quickly injured than any other vital center by shock.

(4) The vasomotor center is not depressed nor fatigued in shock. It is the most resistant of all the vital centers. The peripheral and untraumatized visceral arteries are constricted in shock.

(5) Shock is not due to primary failure of the heart nor to involvement of the cardio-inhibitory or cardio-accelerator mechanism.

(6) It is possible to produce the signs of shock by the use of excessive heat or cold.

(7) The easiest and most certain method of producing shock is by exposure and traumatization of the abdominal viscera. This, judging from the literature, has been the method used by nearly all investigators of shock.

(8) The clinical signs of shock which appear after section of the abdomen and exposure of the viscera are due to a loss of circulatory fluid. This loss of fluid takes place within the tissues and veins of the viscera exposed. The causes for this loss of fluid are apparently the same as those which determine the accumulation of fluid in any other irritated area and produce the signs of inflammation. The nervous system probably plays no greater part in the former case than in the latter. The condition is made grave when the viscera are exposed because of the great vascularity of the tissues involved.

(9) Certain accessory factors which help to produce the condition of shock should be mentioned. These are muscular relaxation, decrease in intra-abdominal pressure and impaired respirations, all of which tend to decrease the amount of blood returned to the heart. The effect of chilling and the use of hot applications should be considered.

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THE GREAT BIG THING IN YOUR SUCCESS AND IN EVERYONE'S SUCCESS IS SPIRIT. IF YOU WANT TO GET BIGGER THINGS OUT OF YOUR WORK, YOU MUST PUT BIGGER SPIRIT INTO IT. YOU CANNOT GET YOUR MAXIMUM RESULT FROM JUST DOING THINGS IN A COMMON, ORDINARY SORT OF WAY. THE AVERAGE MAN'S ACCOMPLISHMENTS ARE FAR BELOW HIS POSSIBLE LIMITS, BECAUSE HE FAILS TO USE THE PROPER SPIRIT IN HIS WORK. WHEN A MAN BUILDS BIG IT IS NOT ALWAYS DONE BY MEANS OF A SUPERIOR INTELLECT, BUT FREQUENTLY BY THE EMPLOYMENT OF A SUPERIOR SPIRIT.

—V. L. Price.

CIRCULATORY DISTURBANCES DUE TO LAPAROTOMY, POSTURE AND ANESTHESIA • ANATOMICAL CONSIDERATIONS • CORELATION OF PRESSURES • SPLANCHNIC STASIS • EXPERIMENTAL CORROBORATIONS • THE EFFECTS OF LAPAROTOMY AND ANESTHESIA ON INTRA-ABDOMINAL PRESSURE • OPERATIVE EXPOSURE AND TRAUMA • TRENDELENBURG AND HEAD-UP POSTURES • PROPHYLAXIS • DEPTH OF ANESTHESIA IN ITS RELATION TO THE PREVENTION OF NECESSARY MUSCLE TONE.

BY WILLIS DREW GATCH, M. D., F. A. C. S. INDIANAPOLIS, INDIANA

UNDER NORMAL CONDITIONS the abdomen contains from 35 per cent. to 40 per cent. of all the blood in the body. The liver alone contains about 29 per cent., and the intestines about 6 per cent. of all the blood. Furthermore, the capillary and venous channels of the abdominal organs are so capacious that they are capable of holding several times the entire volume of the blood.[1] These facts have caused physiologists to regard the splanchnic vessels as the great reservoir for the control of the circulation. Operations which involve direct interference with this reservoir may cause circulatory disturbance of a grave character. It is the purpose of this paper to call attention to the causes of such disturbances and to suggest means for preventing their occurrence.

THE CIRCULATORY ANATOMY OF THE ABDOMINAL VISCERA.

The anatomical arrangement of the abdominal vessels, presents three points of special significance:

1. The circulation through the abdominal viscera is through two sets of capillaries, separated by the portal vein and its radicles. This must slow down the rate of the circulation through the abdominal organs. It is well known that the pressure in the vessels of the liver is very low.

2. The veins of the abdomen have walls so thin that they are easily compressed by the slightest pressure upon them.

3. None of the abdominal veins have valves. How is the flood of the blood through the abdominal organs maintained? We can think of our forces which are involved: These are the force of the heart, the negative pressure of the thorax, the movements of the muscles surrounding the abdominal cavity, and as suggested by Mall,[2] the peristaltic movements of the alimentary canal. It is certain that the force of the heart drives the blood as far as the first set of capillaries. Does it assist the flow beyond this point, or is the flow from here back to the thorax maintained wholly or in part by the other forces?

The key to this problem, it seems to us, is furnished by the behavior of the abdominal circulation when the intra-abdominal pressure is markedly elevated. It has long been a clinical puzzle why patients with peritoneal effusions under great pressure (as high in some cases as 50 or 60 millimeters of mercury) show so little disturbance of the general circulation. It would seem that such a pressure would compress the thin-walled vena cava and other abdominal veins and prevent any flow through them, yet these patients may have no disturbance of circulation in the legs and no abnormal elevation of general blood-pressure.

CORELATION OF PRESSURES

In a series of experiments carried out on dogs, we took simultaneous tracings of the in-

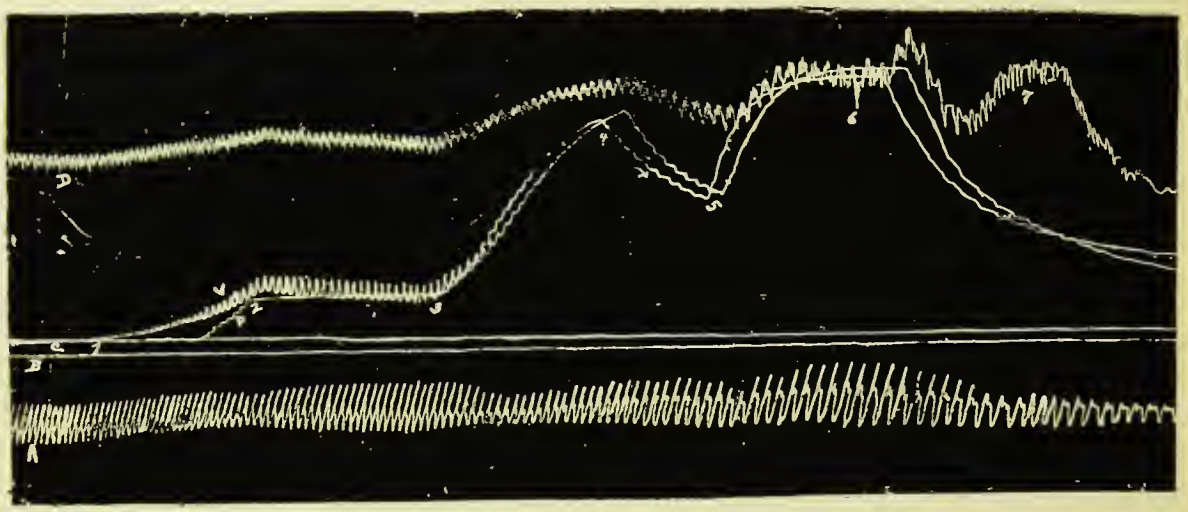

Figure 1 Tracing showing that the intra-abdominal pressure, line *p*, and the pressure in the inferior vena cava, line *v*, are equal. *C*, base line for abdominal and venous pressure. *D*, arterial pressure measured by carotid. The markers which record lines *v* and *p* had to be placed at slightly different horizontal positions to avoid their collision. Note the correspondence of the two curves except at their highest point, due to the fact that here the intra-abdominal pressure is as great as the general blood-pressure and the circulation through the abdomen is failing. In records showing an increase in intra-abdominal pressure to a level slightly below that of the arterial pressure the latter does not rise above the normal level.

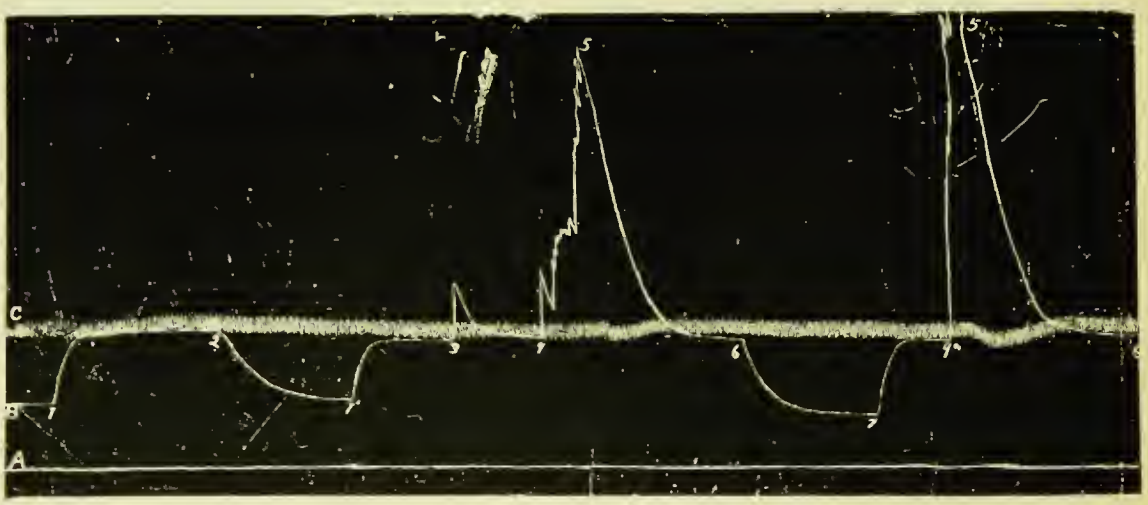

Figure 2. Tracing of the carotid blood-pressure and the pressure in the distal end of a severed femoral vein. *A*, is the base line; *B*, is the end pressure in the femoral vein; *C* is the carotid blood pressure. The femoral artery was clamped at the beginning of the experiment; at 1 the clamp was removed; note that the venous pressure immediately rises to the level of the arterial pressure. At 2 the artery was clamped again, causing a gradual fall of pressure in the vein. At 1 the artery was again unclamped. At 3 and 4 the paw was squeezed but not strongly either time. At 5 the pressure on the paw was released.

trathoracic pressure, of the intra-abdominal pressure, of the pressure of the inferior vena cava, and of the general blood-pressure. The pressure in the vena cava was taken by thrusting a canula up through an opening in the femoral vein. We raised the intra-abdominal pressure by injecting warm salt solution into the peritoneal cavity.

The tracing (Figure 1) shows that the intra-abdominal pressure and the pressure in the inferior vena cava are always equal and rise and fall together. When the intra-abdominal pressure is elevated till it is higher than the blood-pressure, the circulation through the abdomen is abolished, the abdominal viscera being found bloodless at autopsy.

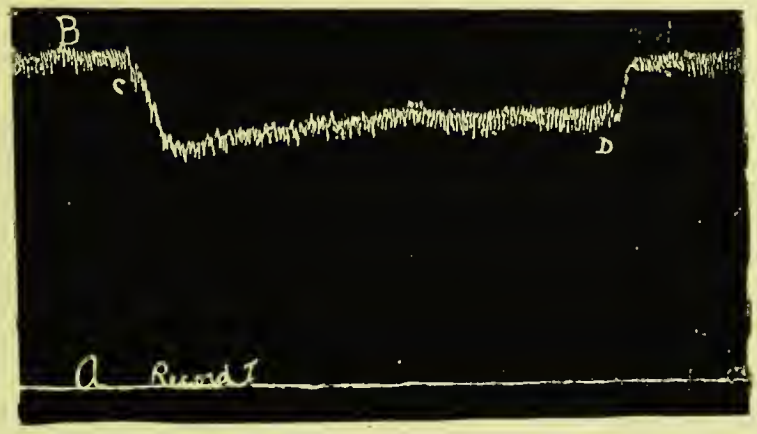

Figure 3. Tracing showing the effect upon blood pressure of the head-up position under ether anesthesia, light enough to preserve a slight degree of tension of the abdominal wall. *A* is the base line, *B* the blood pressure; at *C*, the dog was placed in the head-up position of 60 degrees; at *D* it was placed in the horizontal position. Note the moderate fall of blood pressure and the partial compensation between *C* and *D*.

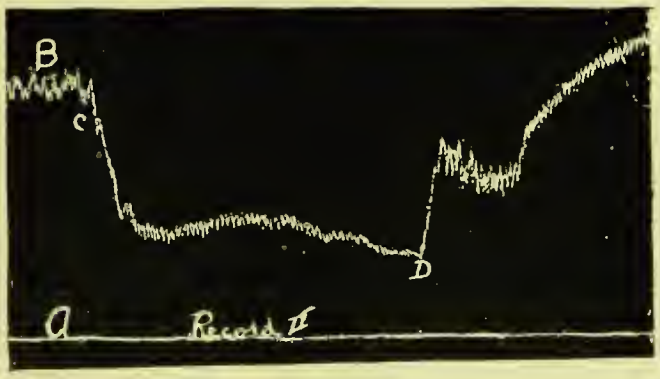

Figure 4. Tracing showing the effect upon blood pressure of the head-up position when complete muscular relaxation had been produced by carare. Dog under artificial respiration. The letters have the same significance as in Figure 3. Note the sharp fall of pressure at *C*, and the progressive fall between *C* and *D*.

What is the explanation of these findings? Suppose that the intra-abdominal pressure be

increased above the venous pressure. The veins will be compressed and no blood will flow through them till enough blood has been forced into them from the arteries to raise the intravenous pressure to the level of the intra-abdominal pressure.

Our experiments have driven us to the conclusion that the chief and essential force which propels the blood through abdominal organs is the beat of the heart. The well-known fact that pressure upon the abdomen increases the output from the inferior vena cava is not evidence against this view, because such increase is not maintained unless the circulation is greatly depressed. The absence of valves in the abdominal veins prevents any variations in intra-abdominal pressure due to movements of the abdominal walls from pumping the blood toward the thorax with any great degree of efficiency, because as soon as the pressure is released there is a regurgitation. That the heart alone is capable of keeping up the abdominal circulation is proved by the experiment we have described. For in this the abdomen was distended till all movements of its walls and of the diaphragm had ceased, and till the intrathoracic pressure was positive most of the time, yet the circulation through the abdomen was maintained. In such a case no force other than the beat of the heart could be in action. The design of nature in not providing the abdominal veins with valves would seem to be to prevent the forcing too suddenly of a dangerously large amount of blood into the thorax.

The action of venous valves and the mechanism by means of which the circulation through the legs is maintained, we showed by the following experiment: Having divided the femoral vein of a dog, we tied the proximal end and attached a monometer to the distal end. At the same time we recorded the blood-pressure in the carotid artery. The pressure in the femoral vein rose to the exact level of the blood-pressure. When we squeezed the paw, this pressure arose to a height several times greater than the blood-pressure (Figure 2.) This experiment clearly shows (1) that the *vis-a-tergo* of the heart unaided can raise the venous pressure to the level of the arterial pressure, and (2) that the valves in the veins of the leg form a device by means of which every movement of the limb which compresses the veins suffices to force blood into the abdomen. No matter how great the intra-abdominal pressure may be, we would not expect venous stasis to occur in the legs, so long as the venous valves are competent, provided there is no cardiac nor renal disease. This conclusion, as far as we can determine, is in accord with clinical observations.

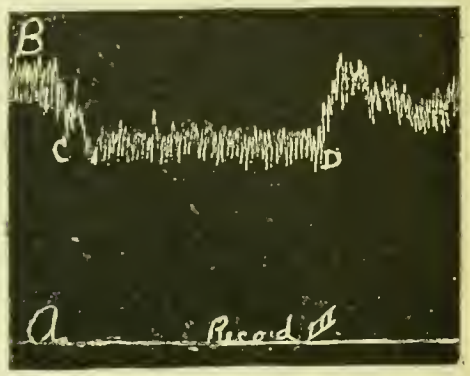

Figure 5. Tracing obtained from a dog paralyzed by curare, into the abdomen of which warm normal saline solution had been injected till the abdominal walls were under slight tension. Lettering the same as in the last two figures. This tracing shows clearly that the fall in blood-pressure in the curarized animal, due to the head-up position, can be prevented in great part by raising the intra-abdominal pressure.

FACTORS CONTROLLING SPLANCHNIC STASIS

Since the splanchnic vessels are capable of holding several times the total amount of blood in the body, it is evident that something must prevent their complete filling. We know of two mechanisms for preventing this. These are the vasomotor apparatus and the contraction of the abdominal muscles. The first acts by decreasing the flow into the splanchnic area, and the second by raising the abdominal pressure, thereby diminishing the capacity of the capillary and venous channels.

The relative importance of these agencies can be determined by deduction from the facts we know about the mechanical conditions of the abdominal circulation, and by direct experiment. The argument from deduction is as follows:

Since the abdominal veins are never filled

to more than a part of their capacity, they must be held in a condition of partial collapse by the intra-abdominal pressure. The blood in them, as we have demonstrated, is under this pressure. The flow through them depends upon the *vis-a-tergo* of the heart, assisted somewhat by the negative pressure in the thorax, and by rythmical variations in the intra-abdominal pressure. If, now, the latter be reduced to that of the atmosphere by weakness or paralysis of the abdominal walls or by laparotomy the force of the heart will continue to propel blood into the veins, but there will be no force in action to drive it out of them till they are distended to their full capacity, because their walls no longer have any external support. But since there is not enough blood in the entire body to distend them to this extent, nearly all the blood will accumulate in the abdomen. It would seem that such an accumulation can be retarded, but not entirely prevented by contraction of the splanchnic arterioles, since it is improbable that such contraction can be so effective as to shut off all flow through these vessels. Under the conditions we are considering, death will soon occur unless the return of blood from the abdomen be assisted by gravity or by pressure upon the abdomen.

EXPERIMENTAL FACTS THAT CORROBORATE THEORETICAL DEDUCTIONS.

That these historical deductions are correct is shown by much direct experimental evidence. It is well known that a hutch rabbit soon dies when held up by its ears.[3] The cause of death has been shown to be the accumulation of blood in its abdomen. Its thin abdomial muscles are too weak to maintain an adequate intra-abdominal pressure. The wild rabbit cannot be killed in this way. A dog when etherized till its muscles are completely relaxed will die in the head-up posture, while it will be little affected by the same if unetherized or etherized lightly. The fatal outcome in cases of this kind can be retarded but not prevented by contraction of the abdominal arterioles. It can be delayed but not prevented by stimulation of the splanchnic nerves and it is hastened by section of these nerves. Figures 3, 4, and 5 show the effect upon blood-pressure of the head-up posture under different degrees of intra-abdominal tension.

We conclude that life is possible when the intra-abdominal pressure has been reduced to that of the atmosphere, only when the return of blood to the heart is assisted by gravity, and when the animal is not required to make any great exertion. It is a fallacy to think that pressure upon the abdomen in cases of failure of the circulation owes its beneficial effect to compression of the arterioles and support of the vasoconstrictor mechanism. Raising the intra-abdominal pressure may perhaps render some support to the vasoconstrictor apparatus, but its chief beneficial effect is due to the partial obliteration of the veins and capillary vessels.

EFFECTS OF LAPAROTOMY AND ANESTHESIA UPON INTRA-ABDOMINAL PRESSURE.

Let us now consider the application of the principles we have just discussed to the question of the effect of laparotomy. Theoretically it may seem that the chief danger of opening the peritoneal cavity arises from the decrease of the intra-abdominal pressure. But in case the incision is not a very large one and that the intestines are not allowed to protrude, the opening, as we have shown by direct experiment, does not affect this pressure to a marked degree. However, if the viscera are pulled out and freely exposed the pressure becomes atmospheric and there is a marked stasis of blood in the abdominal veins, which withdraws a dangerously large amount of fluid from the circulation. Direct pressure by means of large pads upon the exposed viscera is sufficient to correct this trouble, and we advocate that it be employed continuously during evisceration. This means is capable of supplying the place of the normal intra-abdominal pressure. In fact it is so effective a means of returning blood to the heart that it may be, at times, a source of danger, as we have pointed out in a former article.[4]

The effect of anesthesia, so deep as to abolish completely the tone of the abdominal wall, is to promote the accumulation of blood in the abdomen and limbs, and in our opinion, not uncommonly causes a failure of the circulation during and after operation. It is fortu-

nate that laparotomy is nearly always performed with the patient either in the horizontal or in the Trendelenburg position, for if it were usually done with the patient deeply anesthetized and in the feet-down posture many more fatalities would occur. Operations both on animals and on man are much better borne under an anesthesia so light as to preserve the tone of the muscles. This is one reason why there is much less so-called *shock* under nitrous oxid-oxygen anesthesia than under anesthesia due to more powerful agents.

In performing exploratory laparotomy for gunshot wounds of the abdomen, we have several times noted, on opening the abdomen, what we felt certain was a great increase in the hemorrhage from a severed intra-abdominal vein. In one case in which the bullet had wounded the vena cava, there was but little blood found when the abdomen was first opened, but when we raised the transverse colon a frightful gush of blood took place. We have made similar observations in two cases of gunshot wounds of the liver. On theoretical grounds we would expect the hemorrhage from such a source to be increased by laparotomy, for with the abdomen intact the pressures in the vein and that in the peritoneal cavity are equal and but little blood will flow, therefore, from the vein. However, when the peritoneal pressure has suddenly been reduced by laparotomy below that in the vein, active bleeding will occur.

It is well known that patients with large umbilical herniæ are liable to sudden death after operation. It has been suggested by Judd,[5] that the chief cause of this is the sudden increase in the intra-abdominal pressure due to the reduction of the hernia and the closure of the defect in the abdominal wall. He does not give his opinion how such increase in abdominal pressure acts to bring about this fatal result. We are inclined to attribute it to impeded respiration, rather than to direct embarrassment of the circulation, because elevation of the intra-abdominal pressure, even to a great height, does not, in the absence of asphyxia, cause any noteworthy increase in the general blood-pressure.

CIRCULATORY EFFECTS DUE TO OPERATIVE TRAUMA AND EXPOSURE.

We shall consider next the effect upon the circulation of exposure and traumatization of the abdominal viscera. The nature of these effects is shown to every surgeon. Exposure of the intestine to the air causes it to become intensely congested and blue in color. After somewhat prolonged exposure and handling it becomes edematous, and subperitoneal extravasations of blood occur. Microscopic sections of exposed gut or omentum show all the changes characteristic of acute inflammation—in fact some of the classical descriptions of inflammation were derived from such material. There is intense congestion and actual thrombosis of the veins, with margination of leukocytes, edema of the tissues and large and numerous extravasations of blood. *When we take into account that the peritoneum has a surface as large as the entire cutaneous surface of the body we can form some conception of the amount of plasma and blood-cells which may be withdrawn from the circulation by such changes.*

The work of Crile in developing the vasomotor theory of shock has been of immense service to surgery, has stimulated the performance of a great amount of clinical and experimental work, and has led to numerous improvements in operative technic and anesthesia, but the results of Janeway, Seelig and Lyon,[6] Henderson,[7] Mann,[8] and others, have made it no longer tenable.

In the extensive experimental investigation of surgical shock, carried out in the writer's laboratory by F. C. Mann, (See: F. C. Mann: The Peripheral Origin of Shock; herewith printed in the Year-Book), it was found that unless the abdomen be opened it is impossible to reduce a dog to a condition of shock by traumatization alone, if the anesthesia be carefully attended to, and if all hemorrhage be prevented. Severe traumatization alone, without laparotomy, carried out for periods of four to six hours' duration has no injurious effects upon the animal's circulation or respiration. This statement is in accord with the findings of Porter,[9] Hill, and others, and is, we believe, also in accord with every-day observation in human surgery. We must conclude that the

harmful effects of nervous stimuli from the field of operation upon the nervous centers during general anesthesia are almost *nil*. The anesthesia blocks the passage of afferent impulses to the motor cells, and the activity of the vital centres is then controlled, almost entirely by the chemical constituents of the blood.

Mann, after a careful review of the protocols of the experiments of various investigators of shock, could find but few experiments described in which, if the method of producing shock were recorded at all, laparotomy and traumatization of the viscera were not the means employed. The experiments of Henderson, who produced shock by excessive pulmonary ventilation, are an exception to this statement. *Mann arrived at the conclusion that experimental surgical shock is caused practically always by the accumulation of blood in the abdominal viscera. Such accumulation may be brought about by deep anesthesia alone, especially when the same is associated with the head-up posture.* The explanation of this we have already given. Shock of this character is quite easily recovered from because the plasma and blood-cells are still in the vessels, and need only to be forced into the general current of the circulation to bring the patient around. When, however, the viscera have been exposed and traumatized, the fluid and cellular elements of the blood pass outside the vessels, there being a grave injury to the endothelial cells of the smaller channels. Recovery is then more doubtful and its possibility depends upon the amount of blood which has been lost. Seelig and Lyon, Malcolm,[10] Mann, and others, have produced what seems to us conclusive evidence that the visceral and peripheral arterioles are constricted in shock, and that the vasomotor centre is active till the very end. The blood-pressure falls, to be sure, but this is because there is not enough fluid in circulation to maintain it, and happens in spite of the vaso-constriction.

The remarkable experiments of Carrel,[11] with what he terms visceral organisms, have an interesting bearing upon the questions we are considering. In these experiments Carrel removed all the thoracic and abdominal organs from cats and dogs and preserved them at 38°C. in Ringer solution, being careful to prevent any loss of blood and keeping up intratracheal insufflation all the while. The heart continued to beat, but the organs would generally soon become pale and anemic looking. By transfusing blood from a living animal, however, into the organism, the latter would assume a normal color, and the circulation would be completely restored. Carrol succeeded in keeping such organisms alive for from twelve to thirteen hours, and found that the digestion of food, excretion of urine, and other metabolic processes, were carried out by them in a fairly normal manner. He states that after five or six hours, hyperemia of the intestines and peritonitis usually developed, and it appears from his account that this was the cause of death of the organism.

We believe that the following interpretation of the circulatory phenomena observed in these organisms is justified. When the vasomotor tone of the splanchnic arteries is abolished by severance of all connection with the central nervous system, the blood drains rapidly into the capillary and venous channels of the viscera and so much blood accumulates in these that the circulation fails. When they are completely filled by transfusion it is restored, but fails again when inflammatory changes in the intestines permit the exudation of plasma and cellular elements from the vessels. The circulation of a patient reduced to shock by exposure and traumatization of his abdominal organs is in practically the same condition as that of one of these organisms after the peritonitis has developed, for in both cases there is (1) a vasomotor paralysis of the great splanchnic vascular area produced in the case of the patient by the traumatic peritonitis, and in that of the organism by loss of connection with the central nervous system plus the peritonitis; (2) a loss of external pressure capable of keeping the veins and capillaries compressed, and (3) an active loss of plasma and blood-cells due to damage of the endothelial walls of the vessels.

The phenomena of shock and of hemorrhage are practically identical, the only essential difference being that in shock there is a marked fall in the leukocyte count. This is to be accounted for on the evidence of microscopic sections of the exposed and traumatized abdominal organs, by the accumulation of leukocytes in the exposed viscera. Dolley,[12] states that the changes produced by hemorr-

hage and shock in the cells of the central nervous system are identical.

PROPHYLAXIS OF SHOCK—ANESTHESIA, POSTURE, TRAUMATISM.

The conception of the nature of shock which we have just outlined may be termed conveniently the peripheral theory. It will make us combat the occurrence of shock by measures calculated to prevent the accumulation of blood on the venous side of the circulation, especially in the abdomen. In laparotomy there are three chief things to be attended to: (1) the anesthesia, (2) the posture of the patient, (3) the operative procedure.

(1) *With regard to the anesthesia, the depth, from our present standpoint, is the most important thing to consider. The opinion that deep anesthesia is beneficial is a fallacy. Deep anesthesia is to be avoided because it promotes stagnation of blood in the veins. The ideal depth of anesthesia is that at which the troublesome reflexes of vomiting and struggling are abolished, but at which the tonus of the muscles is well preserved. In observations on over a hundred animals and on several thousand human subjects we have never observed any harmful reflex disturbance of either respiration or circulation to occur at this depth of anesthesia. Small variations in blood-pressure may result from traumatic stimuli, but they are in no sense harmful and are not nearly so large as occur almost every moment of waking life. Struggling, vomiting and asphyxia must be avoided.*

(2) We have pointed out in a former paper certain dangers of the Trendelenburg position. The practical conclusion therein arrived at is that this position should not be used in the presence of cyanosis or struggling, and that it should be used with caution in case the heart is diseased. With these exceptions we believe the position to be harmless. It is distinctly beneficial in shock.

(3) The peripheral theory of shock does not compel us to employ short abdominal incisions for fear of lowering the intra-abdominal pressure. It rather, in fact, makes us use longer incisions, for if we keep the viscera inside the abdomen, the intra-abdominal pressure is kept at a level sufficiently high for safety, and less trauma will be done with the long than with the short incision. The theory does compel us to avoid evisceration, and if this is necessary to keep constant pressure on the intestines removed. It is needless to dwell upon the necessity of gentle handling of tissues and keeping the intestines covered.

We have seen the intestines packed off with wet pads steaming hot which were kept at this temperature by frequent wetting with hot salt solution. Experimentally animals may be reduced to a state of shock by this means alone. At autopsy extensive edema of the parts exposed to heat are found and the veins are full of thick tarry blood. It is well known that a rabbit may be killed by immersing only its ears for some time in hot water. The condition so produced by heat seems to be due to a decomposition of the plasma, whereby toxic proteid substances are freed, as is probably the case in burns of the skin.

When the grave inflammatory changes which we have described have taken place over large areas of peritoneum, the treatment of the condition becomes the same as for hemorrhage. Abdominal compression which may be conveniently accomplished by binding a pillow tightly to the abdomen is a valuable measure, since it prevents further loss of blood from the general circulation. It is powerless to restore to the circulation the plasma and blood-cells already in the tissues. Direct transfusion of blood, if possible, is the most efficient remedy.

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ANESTHESIA, ANEMIA AND RESUSCITATION . GENERAL EFFECTS OF PARTIAL AND COMPLETE ANEMIA OF THE CENTRAL NERVOUS SYSTEM AS SEEN IN DOGS RESUSCITATED AFTER RELATIVE DEATH . SPECIAL PHENOMENA FOLLOWING RESUSCITATION . SUMMARY OF RESULTS . CONCLUSIONS . PRACTICAL APPLICATION OF EXPERIMENTAL DATA . CLAMPING THE CAROTID . CONTROLLING CEREBRAL ANEMIA . RESEARCHES OF WYETH . DIFFERENTIAL LIGATIONS . PROPHYLACTIC MEASURES

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THE FOLLOWING STUDIES of anemia of the central nervous system in relation to anesthesia, asphyxia, certain operative procedures and resuscitation, have been made to solve practical clinical problems which the surgeon, anesthetist and internist confront.

In regard to resuscitation of the body as a whole, the fact has not been sufficiently appreciated that the greatest and most essential difficulty is to overcome the anemia of the brain. In apparent death from drowning, gas-poisoning, electric shock or from any of the many other causes of suspended animation, the organ which most quickly succumbs beyond the power of reanimation is the brain rather than the heart. Since continued normal action of the heart and lungs is dependent on the activity of the brain, the presence or absence, as well as the degree and duration of anemia of the latter organ, decides the possibility of resuscitation.

Kuliabko's brilliant work in making the heart continue to beat after its removal from the body, supplemented by the work of Hill, Batteli, d'Halluin and others abroad, and of Stewart and his associates in this country, paved the way for further study of the automaticity of that organ. Attempts to resuscitate the body as a whole by massage of the heart, by artificial respiration or by the injection of saline or other solutions into the circulation were the natural sequences of their results.

The data herewith presented and their practical application to the problems presented by anesthesia, asphyxia, certain operative procedures and resuscitation, are the results of laboratory and clinical experiments in continuation of those already presented on shock, in which it was shown for the first time that the blood pressure of a decapitated dog could be maintained for hours by means of the slow, continuous infusion of normal saline solution and adrenalin. These experiments led naturally to the use of adrenalin-saline intravascular infusion combined with rhythmic pressure of the chest as a means of resuscitation, a method which so far as is known, was first demonstrated by the author before the Cleveland Medical Society at Western Reserve University Medical College.

INTRODUCTORY CONSIDERATIONS REGARDING TOTAL AND PARTIAL ANEMIA OF THE CENTRAL NERVOUS SYSTEM.

For a number of eminently practical as well as scientific reasons it is important to know the effects of total or partial anemia of the brain. Such knowledge will enable the surgeon to make an intelligent decision regarding his operative technic involving ligation of the carotids or pressure on the brain by retractors; or in estimating the damage of the anemia complicating cerebral compression from fractures of the skull, tumors, abcesses or edema of the brain or hemorrhage.

That this knowledge be complete and valuable it is necessary not only to determine but

also to appreciate the differences existing between the resistance of lower and higher cerebral centers to varying degrees of anemia of limited duration. This phase of the subject is all the more vital since resuscitation of the body as a whole after apparent death, does not insure the restoration or integrity of the various intellectual, sensory or motor centers.

In the course of evolution, the brain, more than any other organ in the body, has been evolved in such a way as to have a constant supply of blood under even pressure. Briefly summarized the anatomical points which have a direct bearing on cerebral anemia are as follows: (1) Provision is made for cerebral expansion and contraction within the skull, (2) there is a blood-pressure-raising mechanism with which to combat anemia; (3) the four major arteries (carotids and vertebrals) are placed in the most favorable positions for both active and passive protection against injury; (4) these arteries empty into a circular receiving vessel (circle of Willis) at the base of the brain which equalizes the pressure and from which an even start is made for the passage of the blood through the straight, nonanastomosing arterial trees to every part of the cerebral tissue.

GENERAL EFFECTS OF COMPLETE ANEMIA OF THE CENTRAL NERVOUS SYSTEM AS SEEN IN DOGS RESUSCITATED AFTER RELATIVE DEATH.

In his experiments the author has obviated the disturbing factors of colateral circulation, always present in the technic of occluding either the cerebral vessels or the aorta at various levels, and he has "maintained the integrity of spinal centers, so necessary for the resuscitation of the cerebral centers, (Stewart) nor has the introduction of emboli been permitted to preclude the possibility of recovery studies."

The author's study of brain anemia has been a sequence of his work on the resuscitation of animals killed by anesthetics or asphyxia, the technic of resuscitation being as follows:

By means of a centripetal infusion of salt solution into an artery, together with the simultaneous injection into the stream of one or two cubic centimeters of a 1-1,000 adrenalin chlorid solution, the simultaneous employment of vigorous artificial respiration and rhythmic pressure on the thorax over the heart, the animal may, within certain limits, be resuscitated. For as long as 5 minutes after total cessation of function resuscitation is usually successful; for as long as from 5 to 10 minutes there are more failures; while after 10 minutes the chances of success are progressively less. This method is uniformly successful within the limits which are compatible with the vitality of the central nervous system. This method is also necessarily limited, for in the case of a heart which is losing its irritability owing to the lapse of time, dilatation may occur from the infusion before the beat is inaugurated. Even in dogs with rigid chest walls compression of the thorax proved satisfactory. In periods under 5 minutes but little compression is necessary. Direct cardiac massage, is, therefore, not essential. The primary purpose being to determine the period and degree of anemia which the central nervous system can endure with subsequent recovery, this method offers the advantage that no operative procedure is necessary except the small incision for inserting the canula.

The author's results are based, first, on a series of 30 unselected dogs, resuscitated after the lapse of various periods of time, in all but 5 of which the subsequent course of events was not disturbed. These 5 were killed after different lengths of time for the purpose of histologic examination. Secondly, the series of 60 experiments on dogs, previously reported in the paper on resuscitation, was drawn upon for data pertaining to this work. In the latter experiments blood-pressure and respiratory tracings were made.

TECHNIC OF THE EXPERIMENTS AND RESULTS.

For the recovery experiments, with one exception, the dogs were killed with chloroform. While open to objection on account of the paralyzing effect on the nervous system and nonelimination of the chloroform until after resuscitation, this method was adopted in imitation of the condition most likely to afford opportunity for resuscitative measures in failure of the heart during operative procedures. All operations were done with the customary aseptic precautions. The infusion canula was inserted into the axillary artery.

The period of total anemia was estimated to start from the moment when the first heart sound ceased to be audible with the stethoscope, this sound sometimes persisting for several minutes after the failure of blood pressure as recorded upon the drum and the disappearance of the carotid or femoral pulse and the

second sound. In doubtful cases a leeway of at least one-half minute was allowed from the last distinct sound to the recorded cessation. From the time of starting the chloroform to respiratory failure there was an average of two and three-fourth minutes, with a minimum of fifty seconds and a maximum of seven and five-twelfth minutes.

From a study of the blood-pressure tracings of the first series, while the dictum of Leonard Hill, that: "It is obvious that the cortex can be kept from death for hours by the merest dribble of blood," was not contraverted, still it was apparent that cases with prolonged partial anemia did not recover as readily as did the average dog subjected to total anemia of proportionate duration.

In several instances there was a brief spontaneous recurrence of the heart sounds, occurring from twenty seconds to one and one-half minutes after they had entirely ceased, accompanied in two instances by some faint respiratory efforts, but in only one instance was the carotid pulse palpable. As the total duration of anemia could not be absolutely determined, the absolute and practical duration were both considered and the time spent in resuscitation included in the period of total anemia.

While it seems reasonable to suppose that centripetal arterial infusion of salt solution aided by indirect massage of the heart would hardly reach the brain to any extent during a period of administration of from 1 to 3 minutes, and further, as if it did there would be very little blood in the saline solution, the question was put to the test of experiment. In a dog which had been dead for 12 minutes a solution of methylene blue was infused into the axillary artery, and the usual procedures, with the exception of the adrenalin injection, were carried out for double the average time. No indications of its having reached the bulbar centers was found. This is in contradistinction to direct massage, which according to d'Halluin, supported by the results of Prus, effects a veritable artificial circulation, which is sufficient to reanimate and maintain bulbar activity, although it does not accomplish permanent resuscitation.

In the author's technic of resuscitation, the definition of the period of total cessation of the circulation was, however sharp, the resumption of function on the part of the heart being abrupt and visible as well as palpable. After a few initial heart sounds blood-pressure rose rapidly, often within 10 seconds, to as much as 200 mm. of mercury or over, this rise being due to the adrenalin.

One dog out of 12 with total cessation of circulation between the periods of 7 minutes and 8 minutes and 30 seconds, recovered, whereas only one out of 7 between the periods of 5 minutes and 6 1-2 minutes died apparently as a direct result of the anemia.

Our experiences showed no intermediate condition uncomplicated by accidental organic lesion; in other words no slow decline to death. The demarcation between recovery and death was sharp. In practically all experiments the crisis was reached in from twelve to twenty-four hours. Then death ensued quickly or else distinct improvement of nervous functions began shortly, continuing more or less rapidly until complete restoration, though the convalescent period in some cases lasted from 4 to 6 weeks.

Our results accord with the statement of Leonard Hill, that: "The degree of anemia required to produce dementia is separated by the narrowest line from that which produces coma and death of the respiratory center. There are either no symptoms or death in a few hours." Up to a certain point, not to be exactly limited, but roughly 6 minutes, the after effects are not marked, and the second, third or fourth day brings complete recovery. Beyond the 6 minute limit, however, there is a great deal of after-effect which increases disproportionately with the increase in the duration of the period of anemia, in some instances reaching a state in which the animal is little more than a cardio-respiratory mechanism.

Beyond this limit recovery is altogether uncertain, but our experiments indicate that the stage of depression is tided over and that recovery will be complete eventually, though the narrowness of the escape is shown by the degeneration of a certain number of neurons in the recovered dogs, whose brains were studied by the Marchi method. This does not exclude the possibility of partial recovery with permanent localized after-effects, the degeneration predominating in the pyramidal fasciculus. The distinction here has reference to the ability

of the whole organism to maintain any life. The viability of the vital centers, as well as of other centers, is considerably above that of the brain as a whole, as the recovery results prove, and the immediate outcome must depend on the maintenance of the inter-relation and association of all brain centers, cortical and subcortical. Stewart says that, when exposed to adverse circumstances, the synapse proves the weak link in the nervous chain.

While subject to considerable variation the following is the sequence of return of the various functions and reflexes after resuscitation from relative death; respiration, vasomotor control, corneal reflex, knee-jerk, (tendon reflexes in general,) winking, cutaneous reflexes partial or complete contraction of the pupils and light reflex.

Hypertonicity of the voluntary musculature immediately succeeded the recovery of a normal tone and was manifested by the exaggeration of the knee-jerk, if not by a more or less widespread spastic condition. This hypertonicity always immediately followed the reappearance of the knee-jerk.

Reflex muscular movements, the result of skin or tendon stimulation, always preceded those of spontaneous origin. Spontaneous incoordinate movements appeared sometimes before, sometimes after the light reflexes, but their later appearance occurred only when the light reflex returned relatively early. Succeeding the coordinate movements appeared what may be classed as purposeful movements, attempts to turn over, to arise or to crawl forward—movements involving all the muscles of locomotion. Usually after the appearance of coordinate movements, auditory and visual reactions reappeared, the former being always the more definite and returning first.

The course of events after resuscitation may be summarized as follows: A state of hyperexcitability follows reanimation, reaching its maximum in from one to three hours, when retrogression begins. The second stage is characterized by uncontrolled muscular movements, either coordinate or convulsive, lasts a longer time and passes gradually into the third stage of depression and paralysis, in which the reflexes are more or less impaired.

SPECIAL PHENOMENA FOLLOWING RESUSCITATION.

RESPIRATION—Respiration has recurred in every animal in which the circulation was restored and maintained for a sufficient period. Comparison of the time of restoration of respiration in our experiments shows a much more rapid recovery than that recorded by Stewart, Prus, Batelli. This was probably due to the higher blood-pressure in the author's experiments due to the adrenalin used, for as Hill observes: "a certain arterial pressure is necessary to invoke respiration." In our experiments the average time for the restoration of animals subjected to anemia for periods of from 3 to 8 minutes was 3 minutes and 14 seconds.

The first respiratory gasps were distinct and fairly strong. In the majority of the animals after a few gasps, inspiration exhibited a triple character, with the inspiratory-expiratory ratio of three to one, such as occurs in sobbing. This lasted for several minutes. Gradually the rate increased and the rhythm became regular. A sudden resumption of the normal type of breathing sometimes happened in dogs subjected to short duration of anemia, and was always associated with the simultaneous recovery of the eye reflexes. A rapid increase of rate was the rule in all cases, as much as 100 per minute being recorded, but usually the high rate did not long continue. As the rate slowed a prolonged and labored expiration was characteristic and in some cases a normal rate was not established until the third day after resuscitation.

BLOOD PRESSURE—The use of adrenalin complicated the study of blood-pressure changes. In a successful resuscitation the blood-pressure rose rapidly, often within ten seconds, usually to a height of 200 mm. of mercury and in one instance to 250 mm. This level was usually maintained from two to five minutes, and then it began to fall as the effect of the adrenalin wore off. From 10 to 40 minutes elapsed before the lowest level was reached. Depending on the extent of the vasomotor reactivation, either a tendency to rise was immediately exhibited or the low level persisted for from 10 to 20 minutes, in the latter case with a subsequent rise.

On account of the adrenalin effect in overlapping the normal return of vasomotor activity, particularly after the shorter periods of anemia, the relative time of the reactivation of the vasomotor center could not be absolutely determined. Stimulation of the sciatic nerve did not cause the usual rise in blood-pressure until the secondary rise had begun, and respirations were well established.

With one exception respiration in all experiments returned well before the end of the first fall in blood-pressure. Synchronously with the pressure reaction, respiration rather suddenly assumed a more normal type. It appears, therefore, that the return of vasomotor activity is nearly synchronous with the return of respiration after the shorter periods of anemia, but is more delayed after the longer periods, and no longer occurred after 35 minutes of anemia.

REFLEXES—While varying considerably in the time of their recurrence, after equal periods of anemia, the corneal reflex and spontaneous winking returned in all but three experiments which were not sufficiently protracted. The light reflex reappeared constantly after 8 minutes of anemia, though it was the least uniform in time of its return and in its degree of activity. In periods of anemia of more than 8 minutes the recovery of the light reflex was inconstant. The maximum anemia period after which the corneal reflex reappeared was 24 minutes, and for the light reflex the maximum time was 14 1-2 minutes.

The knee-jerk varied the least in its recovery periods. It was always noted in the resuscitation after the maximum anemia period. Not infrequently there was a difference in the time of recurrence of the bilateral reflexes, in two cases one corneal reflex reappearing three minutes before the other, though for the knee-jerks no difference of over one-half minute was noted. As to the relative time of the reappearance of reflexes, the knee-jerk usually appeared before the corneal reflex, the corneal reflex always preceded spontaneous winking, while in every case the cutaneous reflexes returned before the light reflex.

TEMPERATURE—While not recorded as a matter of routine, sufficient data have been obtained to indicate that the temperature continues to fall for several hours following resuscitation. The lowest rectal temperature was 32.9 degrees C. 4 hours after anemia of 9 1-4 minutes, and 33.8 degrees C. was reached in 16 minutes after 13 1-3 of anemia. From this point the temperature gradually rose to a state of hyperpyrexia, which was more marked in the animals which succumbed. In the dog which recovered after the maximum period of anemia, the maintained level was reached the second day.

PHONATION—9 1-4 minutes of anemia was the maximum period after which this faculty returned. Actual barking, indeed, occurred in but one other case of over 7 1-2 minutes of anemia, though there was whimpering or imperfect attempts at vocalization in three cases. Phonation usually occurred synchronously with or shortly after the exhibition of spontaneous muscular movements, that is one-half to one hour after resuscitation following anemia of 7 minutes.

MICTURITION AND DEFECATION—Micturition or defecation occurred in the majority of animals during the period of hyperexcitability.

AUDITORY, VISUAL AND OLFACTORY SENSES—As already indicated, the reaction of auditory stimuli was definite and unmistakable during the period of hyperexcitability in the recovery dogs, while to various visual stimuli during the same period, the only response was a lid or pupil reflex, but out of 15 animals subjected to anemia for 7 minutes or more, only 6 gave even a temperorary recovery of hearing. Further in animals which recovered the later effects on vision were much more marked, in general increasing as the limit of possible recovery was approached. The sense of smell came back at a point between hearing and vision, though the test was never definite unless irritating fumes were employed.

PHENOMENA REFERABLE TO THE CORTEX—Most of the animals which recovered passed through a final stage comparable in many respects to the condition of Goltz's decerebrates. Such a period was characterized by dementia and loss of intelligence, the lack of any psychic response to stimuli, and the inability to recognize food and drink. Response to stimulation was purely reflex, or was absent if memory of past experiences was involved. Power to localize stimuli was of gradual acquirement. Restlessness, however, was not generally observed.

The temporary paralysis was of cortical origin and was indicated by the associated exaggeration of the knee-jerks. The motor function did not suffer as much as the sensory; for the paralysis disappeared before the return of intelligent and normal response to stimulation. The clinical observation that the cortex suffered the most and was the last to recover is supported by the fact that the histological alterations were more marked in the cortex than in the lower centers.

The other dog which recovered also gave a picture of degeneration, but of a different character. While the actual number of nerve fibers involved was greater, not only was there no localization but there was an early stage of degeneration with droplets of varying size, scattered in longitudinally cut spinal nerves at intervals along the course of the fibers affected. This animal, which was killed in 6 days, was at the time of death, partially blind, deaf and though it could stand, it was too paralyzed to maintain the upright posture or to walk. The question arises as to whether it would have eventually recovered. Judging from the other animals, which, with final recovery, passed through a similar condition somewhat more rapidly, and from the fact that there was a noticeable improvement from day to day in the animal just mentioned, general recovery with complete destruction of a few neurons, is probable.

An early degeneration similar to that mentioned occurred in the fatal cases, though the number of fibers involved was considerably less. None of these animals had lived over 36 hours at the outside. On account of the shortness of the time which had elapsed this appearance was unexpected and will be further investigated. However, it corresponds with the organic changes in the cell-bodies which occurred during the same time.

SUMMARY OF RESULTS.

To determine the limits of recovery after total anemia of the central nervous system, 30 dogs were killed by chloroform and resuscitated after the lapse of varying periods from 3 to 14 minutes. If resuscitated in less than 5 minutes the recovery of function was rapid and was strikingly free from the after-effects which characterized longer periods. Of 7 animals anemic from 5 to 6 1-2 minutes, only one died apparently as a direct result of the anemia, but of 12 subjected to anemia of from 7 to 8 1-2 minutes, only one recovered after 7 1-2 minutes of anemia. The remaining dogs all died.

Histological examination both of presumptive recoveries and fatal cases was made by ordinary methods and by those of Nissl and Marchi. The neurocytes of the fatal cases presented the greatest change, being not only chromolytic but here and there definitely indicative of cell death. Marchi's method further supports these findings by proving the existence of fiber degeneration. Finally showing the narrowness of the escape, in the animal showing the best recovery-result after 7 1-2 minutes of anemia, which at the end of 4 weeks had apparently entirely returned to a normal state, histological examination by the Marchi method showed the degeneration of a number of fibers in the pyramidal fasciculi, which were traced from the cord to the cortex and in Flochsig's fasciculus, while a more sparsely scattered degeneration of both ascending and descending fibres was evident elsewhere.

CONCLUSIONS.

(1) In dogs lightly anesthetized with ether and then killed quickly by chloroform, the average limit of total cerebral anemia, estimated from cessation of the heart sounds to return of circulation, which admits of recovery, is between 6 and 7 minutes. The ulterior limits appears to be under 10 minutes, hitherto stated as the most conservative figure, and any recovery after more than 7 1-2 minutes of total anemia would be exceptional.

(2) Further experience with the resuscitation of animals killed by anesthesia and asphyxia, embracing numerous unrecorded experiments, as well as those forming the basis of this article, establishes the former conclusion of the author and his associates that the arterial infusion of saline-adrenalin solution with rhythmic compression of the thorax over the heart and artificial respiration, affords a reliable method of resuscitation within its limitations, and one uniformly successful within

the limits compatible with recovery of the central nervous system.

PRACTICAL APPLICATION OF EXPERIMENTAL DATA.

The results of our studies in surgical anemia and resuscitation find their most vital and practical application in the solution of the problems confronting the surgeon and anesthetist, during operative procedures involving ligation of the carotid arteries.

From the anatomic relationships it necessarily follows that ligation of the innominate artery would shut off entirely *direct* circulation from the *right* side of the brain. Likewise ligation of the common carotid and of the subclavian proximal to the origin of the vertebral from the subclavian would completely shut off *direct* cerebral circulation on the side on which the ligation was dune.

If the common carotids and the vertebral arteries of *both* sides are ligated the remainder of the collateral vessels must take up the burden—a burden, which for practical purposes is beyond their capacity. It is almost incredible that an individual could live for any length of time after such ligation, though, Erichsen mentions a case of Davy's in which life was maintained for "a considerable length of time."

In ligating *either* common carotid artery success may depend on the patency of the circle of Willis, and while its absence may be extremely rare, Derby describes such a case, in which hemiplegia followed ligation and at the autopsy the circle of Willis was found actually absent.

Granting that the circulation through the four major arteries, (carotids and vertebrals) is alone efficient to maintain the life of the brain, and that ligation of one common carotid leaves the three other vessels still open, still it by no means follows that only one-fourth of the blood supply is cut off, since the common carotids are much larger than the vertebrals. Consequently it is not strange that ligation may cause immediate or remoter catastrophies.

While aseptic surgery has improved the statistics of ligation of the carotids, the sequelae following operations under the most favorable circumstances, still make this procedure an extra-hazardous risk. Hemiplegia of the opposite side is an ever impending catastrophe, and appears in 8.4 per cent. of 500 reported cases, in which 6.8 per cent. proved fatal and the remainder showed recovery with either permanent or transient paralysis. While a few cases of fatal termination have been traced to emboli or thrombi, in the majority of instances, the cerebral injury is due to the anemia, following the ligation, just as in ordinary cases of apoplexy the lesions are caused by anemia, and it matters little where the obstruction is as long as the blood supply is completely shut off or reduced to a destructive degree.

In regard to the local conditions in the brain itself, autopsy reports almost invariably state that *cerebral softening* was present on the side on which the ligation was made. In most cases the softening seemed to be throughout the hemisphere, although in a few cases it was localized.

In considering the etiology of cerebral injury after ligation of the common carotid it may be stated at the outset that the *dangers accompanying surgical interference with the circulatory system of the aged are in direct proportion to the age of the patient.* In the 500 cases studied in almost 61.0 per cent. the control of hemorrhage was the object sought. The high mortality attributed by certain authors to ligation should probably be attributed in great part to shock, hemorrhage and infection. There is evidence of but few cases of serious injury to any of the organs of the special senses, due to ligation alone. Narrowing of the pupil followed by permanent dilatation and dimming of the eyesight may follow.

It has been found that the time of occurrence of cerebral symptoms in relation to the time of ligation varied considerably. Quenu and Verneuil report cases in which hemiplegia occurred immediately after the ligature was tightened. In other cases cerebral symptoms occurred in from 12 hours to 34 days; although it was consistently observed that the older the patient the earlier the cerebral symptoms occurred.

TECHNIC OF LIGATION OF THE COMMON CAROTID ARTERY AND ITS BRANCHES.

Formerly ligation of the common carotid artery was sometimes done, when the compara-

tively modern procedure of temporarily closing the vessel would have better served the interests of the patient. The author has repeatedly demonstrated that, when properly done, an artery may be closed temporarily without injury for as long a time as is ever required for an operation. Consequently certain operations on the head, for example, in which hemorrhage is troublesome, can be done with much greater ease and safety by temporary closure of the common carotid. By this procedure the local field is in better condition for the careful dissection which is so often necessary, and the danger of harmful cerebral anemia is almost completely avoided.

Moreover, *as a preliminary step to permanent ligation temporary closure should be done whenever possible.* There are very few cases in which it cannot be done, and the occurrence of harmful immediate symptoms can be taken as a warning against making a permanent ligation.

The following observations constitute a brief resume of the author's experimental work to determine the effect of a temporary closure of the carotid. The immediate effect on the circulation of the temporary closing of one carotid artery was to increase the blood pressure, but usually a compensation followed, and the pressure returned to its normal level. No effect upon the respiration was observed. The simultaneous closure of both carotid arteries produced a greater rise of blood pressure, which also by physiologic compensation usually soon returned to the normal level. In many of the latter experiments there was a decrease in the respiratory action, although the effect was very slight. In no instances were any striking results noted. In the recovery experiments no effect upon the animal was observed beyond that attributable to the anesthesia and the operation in cases in which the clamps were allowed to remain on the arteries. The animals seemed playful and strong. Even after 24 hours of complete closure there was but little microscopic evidence of injury to the vessel wall. Circulation through the clamped portion was readily reestablished. However, in cases in which the animal had suffered infective inflammation of the wound during the application of the clamps for a considerable length of time, say for 2 days, the damage to the vessels walls was marked, and in some cases the lumen occluded. As to the after-effects, in no case was there any clotting; the aseptic cases made good recoveries; the circulation was reestablished; and no impairment of consequence followed. The cerebral vessels were carefully observed at autopsy, and in no case were either emboli or thrombi found, nor was there noted any gross effect on the brain.

In the course of clinical operations the author has temporarily closed the common carotid artery 136 times. The ages of the patients ranged from 7 months to 69 years. In every instance the circulation was resumed as soon as the clamps were removed. There were no appreciable late affects on the vessel wall at the point of clamping and none on the circulation in the closed arteries or their branches. *Less anesthetic was necessary in those cases in which both common carotids were closed.* The respiration might be embarrassed, but was relieved by partially releasing the pressure on one or both vessels. The operation time was much diminished as a result of the freedom from hemorrhage of the operative field and the amount of blood lost was much lessened, as was the difficulty of keeping blood out of the respiratory tract.

In the closure of the common carotid artery, a valuable clinical procedure is to transfer the clamp to the external carotid as soon as the latter vessel is reached as, for example, in block dissections of the neck. In elderly subjects, especially those with atheromatous arteries, distinct cerebral impairment, amounting even to mild delirium, may appear after temporary closure of the common carotid artery and last for several days, but apparently no permanent damage is done to the brain. Since the adoption of this method of closing the external carotid artery from the beginning of the operation and transferring the clamp in the course of operation, no functional impairment of the brain has been observed.

In the author's experience closure of the common carotid artery does not arrest hemorrhage as completely as does closure of the external carotid. The reason is that when the common carotid is closed and the eternal is open there is a back flow of blood via the anastamoses in the circle of Willis. This explains

why rather free hemorrhage may be seen when the common alone is closed. The best control of all is secured by closing both external carotids.

In his own series of cases, the author has observed no instances of embolism or thrombosis as a secondary result of the temporary closure of either common or external carotids.

As a general principle it stands to reason that, other factors not interfering, the ligation of the large artery should not be done when a small branch of the same vessel can be reached, the closure of which will control the bleeding. In regard to the carotids no one has emphasized this more strongly than Wyeth. In his classical "ESSAYS IN SURGICAL ANATOMY," published in 1878 he says: "I cannot conclude the surgical anatomy of these arteries without protesting with all the earnestness I may possess against the operation of tying the *common carotid* for lesions of the *external carotid or its branches,* when this last vessel may be ligated.

The following extracts from Wyeth are pertinent in establishing the ligations of election in certain operative procedures and in preventing surgical anemia, in so far as its incidence can be controlled:

"(1) In all *intracranial* lesions involving alone the *internal carotid* or its branches this vessel should be tied. If this procedure is not successful then the external carotid should be secured at the crossing of the digastric. If the *facial* be given off below this point it should be secured by a separate ligature . . . . For lesions of the *internal carotid* in the neck (except aneurysm) it should be tied above and below the lesion in all cases. The operation on the cardiac side alone, be the *common* or *internal* trunk the seat of ligature, is not justifiable, death having occurred in many instances through the descending current from the circle of Willis. In aneurysm of this artery, the single ligature on the cardiac side will suffice.

"(2) When the lesion (excepting aneurysm) exists within one-half inch of the bifurcation of the *common* carotid, involving this vessel, or the *external* or *internal,* or both, the *common* trunk must be tied on the cardiac side and the other arteries on the *distal* side of the lesion. The superior thyroid and any other branches of the *external carotid* between the ligature upon this vessel and the bifurcation should also be secured. In case of aneurysm in either of these points the single ligature on the cardiac side will usually suffice.

"(3) In erectile or pulsating tumors of the orbit (intraorbital aneurysm) ligature of the *common carotid* is to be advised . . . . Since anastomoses between the terminal branches of the *external* and *internal* carotids through the orbit, are more or less exaggerated in intraorbital aneurysm . . . . I am of the opinion that the ligature on the *common carotid* is the surest and safest operation.

"(4) Wounds of the *superior thyroid* artery too near its origin to permit a ligature on the cardiac side of the lesion require deligation of the common, external and internal carotids, and torsion of the distal end of the wounded vessel.

"(5) In *incised, punctured, lacerated* and *gunshot* wounds of the *external carotid* or its branches where it is deemed inexpedient to secure the vessel at the seat of injury, the *external carotid should be secured* below the origin of the *lingual* . . . If the *lingual* or any other branch is in immediate contact with the ligature it (or they) should also be secured. The *common* trunk should not be tied under such circumstances *except as a last resort.*

"(6) Hemorrhage of the *tonsils* and *pharynx,* if not arrested by ligature of the *external carotids* as advised, will require either the separate ligature of the pharyngeal ascendens or of the common and *internal* carotids.

"(7) It must be assumed that when the ligature of the *external carotid* below the origin of the lingual does not arrest hemorrhage from the pharynx the bleeding is from the *ascending pharyngeal,* and that this branch originates from the bifurcation of the internal carotid . (One or two deaths have occurred from hemorrhage from the tonsils after ligature of the *common* trunk *alone.*)

"(8) Aneurysm of the *external carotid* or its branches (excepting the *superior thyroid*) demands deligation of the *external carotid alone* when a sufficient space exists between the tumor and the bifurcation to admit the ligature with safety.

"(9) Aneurysm of the *internal carotid* should be treated by ligation of this vessel alone, where there is sound artery enough between the tumor and the bifurcation to admit the ligature with safety.

"(10) Aneurysm of the common carotid (if digital compression shall have been abandoned) should be treated by ligature of this vessel as far from the tumor (on the cardiac side) as possible.

"(11) Ligature of the *common carotid* for aneurysm of the *arch of the aorta* is of doubtful propriety .

"(12) Ligature of the common carotid alone for the cure of innominate aneurysm is an exceedingly dangerous procedure; 12 of 17 cases proved fatal from the operation; only 2 were cured . . .

"(16) In epilepsy, while the danger of death as a result of this operation is comparatively slight, (5 per cent.) the proportion of *cures* or *improved* cases is not great enough to commend this procedure .

"(17) In persistent and exhaustive neuralgia of the fifth nerve when all other methods have proved ineffectual ligation of the *common carotid* should be practiced. The *external carotid* of one or both sides should first be tied below the lingual (the point of election). If this fails the *common* trunk on the affected side may be secured. The operation is contraindicated when pressure upon the *common carotid* of the affected side does not arrest the pain.

"(18) In *hemiplegia or headache* the ligature of the *common carotid* is not justifiable "

Facts like the foregoing furnish an invaluable basis for the control of hemorrhage—one of the most important parts of the surgery of the head and neck. Their value in preventing surgical anemia as far as possible lies in the light they throw on how best to avoid closure of arterial trunks—a secondary, but important

matter. In addition, while the weight of evidence is overwhelmingly against the probability that ligation of the external carotid may cause harmful cerebral anemia, it must be remembered that Scudder has reported a case of hemiplegia with occlusion of the left middle cerebral artery and extensive brain degeneration, and death occurring six days after this procedure.

SUMMARY.

The histologic evidence that even in so-called *recovered* animals, some or even many nerve cells are permanently lost and that all are temporarily damaged explains the great temporary and lesser permanent loss of power following any grave anemia of the brain.

It argues against the practice of permitting the blood pressure to fall extremely low in cases of hemorrhage before resorting to transfusion. It warns the surgeons to be cautious in ligating or temporarily closing the common carotid artery in aged subjects. It warns him not to press against the brain with retractors and packings unless the pressure is made strictly intermittent, never exceeding 5 minutes at a stretch. It explains the reason why in all types of brain pressure the early depression of the higher functions, such as associative memory, occurs before the depression of lower functions such as respiration and circulation. It emphasizes the significance of the gradual onset of dullness and stupor in increased intracranial pressure. It fixes an absolute limit to the possibility of resuscitation in cases of drowning and asphyxia or the toxemia of anesthetics, which makes one doubt the authenticity of many reported cases of resuscitation after apparently long intervals of suspended animation.

IT IS INDISPUTABLY EVIDENT THAT THE GREATER PART OF EVERYMAN'S LIFE MUST BE EMPLOYED IN COLLECTING MATERIALS FOR THE EXERCISE OF GENIUS. INVENTION, STRICTLY SPEAKING, IS LITTLE MORE THAN A COMBINATION OF THOSE IMAGES THAT HAVE PREVIOUSLY BEEN GATHERED AND DEPOSITED IN THE MEMORY. HE, WHO HAS LAID UP NOTHING, CAN PRODUCE NO COMBINATIONS. THE MORE EXTENSIVE, THEREFORE, YOUR ACQUAINTANCE WITH THE WORKS OF THOSE WHO HAVE EXCELLED, THE MORE EXTENSIVE WILL BE YOUR POWER OF INVENTION, AND, STILL MORE LIKE A PARADOX, THE MORE ORIGINAL WILL BE YOUR CONCEPTIONS.

—*Sir Joshua Reynolds.*

BLOOD PRESSURE UNDER ANESTHESIA • GENERAL CONSIDERATIONS • TECHNIC • POINTS IN PHYSIOLOGY • SYSTOLIC, DIASTOLIC AND PULSE PRESSURES • FACTORS AFFECTING THEIR INTEGRITY • RESPIRATION • INTERPRETATION OF READINGS • EFFECTS OF VARIOUS ANESTHETICS • SHOCK • RELATION OF PULSE AND PRESSURES • CAUSES OF LOWERED PRESSURES. • UNNECESSARY PROCEDURES • CONCLUSIONS

BY E. I. McKESSON, M. D. *TOLEDO, OHIO*

IN THE VOLUMINOUS LITERATURE on blood pressure but little is to be found of practical value bearing upon its routine use during surgical or dental operations.

The anesthetist is expected to know his patient's condition at all times, and he is moreover the only member of the surgical team who is at liberty to make the necessary tests to obtain such information. A close co-operation between surgeon and anesthetist in the interest of the patient is essential if the best services are to be rendered.

GENERAL CONSIDERATION.

The anesthetist should know as much as possible of the history of the case, and of the physical fitness of the patient for operation. Perfunctory examinations of the heart and lungs, which give no information of value, should be replaced by such observations as will actually determine something definite concerning circulatory and respiratory efficiency. A few well directed questions concerning dyspnea, nasal or other obstructions, an inspection for edema, sclerosed vessels, an estimation of the systolic and diastolic pressures, and their relation to the pulse rate, are infinitely more valuable than the mere oscultation for heart murmurs.

Blood pressure represents one of the diagnostic means which is of great value if intelligently used, during the course of an operation. The information which it furnishes, not only directs the surgeon and anesthetist to the dangers of overdosage with the anesthetic, roughness in handling the viscera, and trauma caused by gauze packs, all leading to surgical shock, but it definitely shows the gradual development of shock so far in advance of its serious consequences that treatment may be instituted, or the causes modified in such a way as to avoid its complete development before which time no other means than the sphygmomanometer will positively warn us of its onset.

The routine use of blood pressure observations will call into account many points in technic which are now commonly doing the patient injury but are accepted as satisfactory without tests.

TECHNIC.

The method employed for the determination of the blood pressure during an operation differs but little from the oscultatory method ordinarily used. The only difference being in the method of applying the cuff and the stethescope so that they may remain applied to the arm throughout the operative period.

The aneroid type of instrument is preferable for the anesthetist for obvious practical reasons. It is as accurate as the mercurial type and more likely to be accurately read. The stethescope should be an inch and a quarter in diameter, of the diaphragm type, and provided with a ¾ inch garter of sufficient length to pass around the arm and buckle, holding the stethescope just snugly against the skin. A rubber tube about 2 ft. long of suitable size connects the stethescope to appropriate ear

pieces. A similar length of tubing connects the sphygmomanometer with the cuff, which is applied to the arm so that the tubing passes over the patient's shoulder.

Without disturbing sterile drapings, the anesthetist is at liberty to make readings at 5 to 10 minute intervals without inconvenience to himself or surgeon. The readings may be charted by the graphic method, which facilitates the interpretation at a glance.

With the cuff and stethescope applied, the pressure is pumped up in the cuff while listening for the first maximum tone, which is the probable diastolic pressure, making a mental note of the same. The pressure is further increased until the pulse can no longer be heard, noting the point at which it vanishes as the probable systolic reading. Upon releasing the pressure the more accurate readings may be obtained, using the former observations as a guide and index for close attention. The *true systolic pressure* is marked at the point at which pulse tones are positively heard, while gradually releasing the pressure in the cuff, which had been previously inflated well beyond the systolic reading. The pressure is then quickly dropped to within a few mm. of the probable diastolic pressure and then slowly released until the maximum tone heard, changes fairly abruptly to a dull pulse beat, which is the diastolic pressure.

When taking the first reading before the patient has been anesthetized, it is well to corroborate the oscultatory reading of the systolic pressure by palpation of the radial artery. It will usually be observed that the systolic reading will be made from 2 to 4 mm. higher by oscultation than by palpation. Oscultation is considered the more reliable and accurate method.

Between determination, all air should be allowed to escape from the cuff so that circulation will not be interfered with in the arm.

Attention should be given to the phase of respiration in which the readings are taken, because during inhalation arterial pressures are often considerably lower than in exhalation, so that if one reading is made in exhalation and the next reading charted in inhalation, an error amounting to as much as 30 mm. of mercury may occur in extreme cases. For the sake of ease and uniformity, all determinations should be made in exhalation and respiratory pause, disregarding all tones heard during inhalation.

POINTS IN PHYSIOLOGY.

It is not the purpose to deal exhaustively with the physiology of circulation, but to briefly state a few pertinent points relative to the maintenance of blood pressure.

Muscular tissue is the basis of circulation and the production of blood pressure. Its distribution in the vascular system varies, being of course most abundant and highly developed in the heart where it is cross-striated in type. The greater vessels are poor in muscular tissue, but rich in elastic and connective tissue; the smaller arteries and arterioles are largely muscular, but here the muscle is the long striated or smooth muscle, being exceedingly elastic, slower in its contraction, readily stimulated by a mechanical stimulus, and thrown into tetanic contractions by a comparatively slow stimulus, with such contractions in proportion to the strength of stimulus. It is readily observed, therefore, that the characteristics of the smooth muscle of the arteriole differ vastly from those of the cross-striated of the heart.

The quick maximal contraction of the heart delivers a pulse wave to the arterial system, which stimulates the muscle of the arteriole by sudden stretching; the contraction which results being in proportion to the stimulus. Before the arteriole has again relaxed another pulse wave stimulates it to renewed contraction, thus maintaining a certain muscular tonus quite independent of the vasomotor system for the regulation of the caliber of the arterioles by groups or organs during physiological activity.

An idea of the distensibility of the small artery, or the relaxation of smooth muscle, may be obtained from the fact that it is capable of a 45 per cent. shortening in one contraction, and of more than 50 per cent. in tetanic contraction. Applying this figure to the small artery to the appendix, which is about one mm. in diameter when relaxed, we find that the area in that condition is .7854 square mm. A 45 per cent. shortening of the circular muscle would reduce the area to .2376 square

mm. or a 70 per cent. reduction in a single contraction, and a still greater reduction in tetanic contraction.

As a result of this property the great dilitation in the arterial system for the accommodation of the ventricular discharge does not take place in the wall of the great arteries, as popularly supposed, but in the smaller branches and arterioles. As is well known, the combined capacity of the arterioles, capillaries and veinules, is several times the volume of blood contained, and in order to have a positive pressure on one side of the capillaries the arterioles must restrain the flow of blood by their tonic contraction. Even the capillary has power of contraction, although not provided with muscle, so also have the veins, which, however, play a more passive role in the maintenance of blood pressure.

SYSTOLIC, DIASTOLIC AND PULSE PRESSURES.

During normal life fairly constant pressures are maintained in the arterial system at the end of systoles and diastoles, which are recorded as the systolic and diastolic pressures. The difference between the systolic and diastolic pressures represents the amount of increased pressure by each heart contraction, commonly known as the pulse pressure, or stroke. The normal stroke of the heart in mm. of mercury is equal to one-half the diastolic pressure, which, however, does not mean that in an abnormally high or low blood pressure that the existence of this ratio would indicate a normal vascular system, since the heart with high pressures would be overworked, even though the stroke-diastolic ratio were as one is to two.

FACTORS AFFECTING THE INTEGRITY OF THESE PRESSURES.

The rate of blood flow is modified by the pulse rate, the blood pressures, and the contraction volume or discharge of the ventricle. It represents quite an incalculable factor from a clinical point of view, since the volume of blood moved at any pulse rate may vary according to the cardiac tone, or relaxation of the ventricle.

An important element in the maintenance of blood pressure is found in the nourishment of the heart which takes place in diastole, and although lower pressures than those normally encountered in the aorta are adequate in forcing the blood through the coronaries, nevertheless a normal heart will not survive exceedingly low pressure for many hours, for two reasons: (1) Under low pressure conditions the heart contractions are rapid; the diastolic periods being correspondingly shorter permit of less time for the flow of blood through the coronaries and the nourishment of the muscle. (2) Through the rapid contractions the reserve energy of heart is gradually used up, resulting in heart fatigue or decompensation.

If the heart through rapid contraction is unable to increase the blood pressure because of some influences which may be dilating the arterioles, a vicious circle will soon be established by increasing heart fatigue, reducing the efficiency of the heart, resulting in malnutrition, which in turn further decreases efficiency and increases heart fag and results in absolute heart failure.

THE INFLUENCE OF RESPIRATION.

The influence of respiration upon the movement of the blood and the maintenance of blood pressure is quite commonly overlooked. By straining at stool the systolic pressure in an adult may be elevated as much as 30 mm., which may be considered a safe temporary fluctuation in blood pressure. The relation between the thoracic cavity and the heart cavity is similar to a two phase pump; the thoracic cavity playing the part of the large low pressure cylinder; the heart, representing the small high pressure cylinder. During inhalation there is a negative pressure in the thoracic cavity, which sucks the blood from the great veins and delivers it to the right heart and into the pulmonary system where, because of the dilitation of the pulmonary capillaries under a negative pressure, a considerable volume of blood rests until the beginning of exhalation, when the thoracic pressure is changed to a positive pressure, and the excess of blood squeezed forward into the left heart and the great arteries, elevating the blood pressure.

INTERPRETATION OF READINGS.

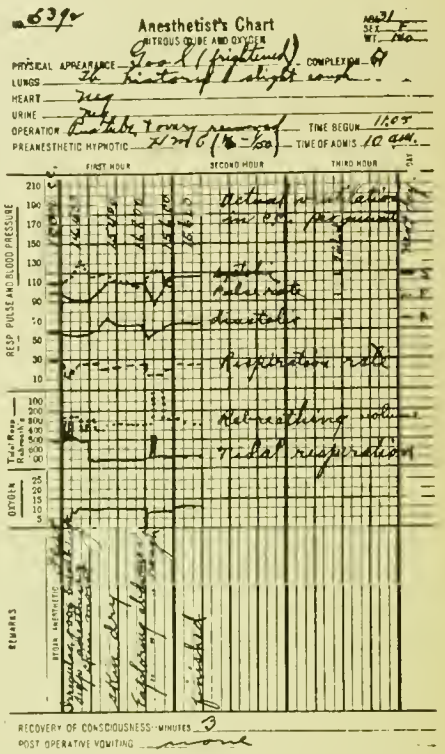
It is a comparatively simple procedure to obtain quite accurate readings by the method previously described, but their interpretation is often more difficult because of the many factors at work which have a tendency to vary the interpretation in any patient under operation. One must consider the physical state of the patient, age and habits with reference to the accepted normal readings, which cannot be discussed here. The nature of the operation, the skill with which it is performed, the anesthetic agent used, the length of time of the operation, together with the skill used by the anesthetist are factors of paramount importance, bearing upon the interpretation of the readings and the prognosis from time to time throughout the operation.

Aside from the diagnostic significance of the blood pressures prior to operation, the anesthetist accepts the patient with whatever pressures are presented, and aims to so conduct anesthesia and to keep the surgeon informed, that the patient may emerge from the operation, if possible, without deleterious effect.

It is at once seen that the blood pressures at the beginning of the operation become the standard for future comparison throughout the work. Any changes from these pressures have a diagnostic importance relative to the efficiency of the circulation. But because of the influence of fear or anxiety just previous to beginning the anesthesia, the blood pressures are often abnormally low, and occasionally unusually high for the particular patient, so that these pressures do not fairly represent the patient's normal, which should have been taken at some time previous. When the patient's normal pressures are not known, the first determination after unconsciousness is secured must then serve as the standard pressures.

EFFECTS OF VARIOUS ANESTHETICS UPON BLOOD PRESSURES.

None of the general anesthetics are capable of producing and maintaining increased blood pressures. As has been repeatedly shown the fall in blood pressures as a result of anesthesia vary with the different agents used, chloroform causing the earliest and most abrupt fall, by a reduction in the pulse pressure as well as the diastolic pressure; ether exhibits a similar action to chloroform, though later in develop-

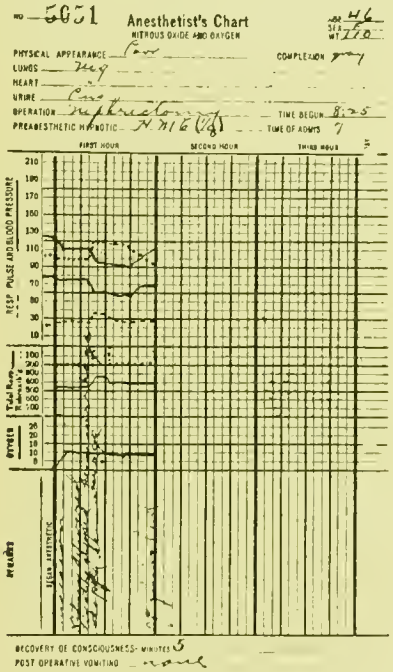


Case No. 5392 illustrates several things. In the first place the patient had too small a dose of morphin and hyoscin for her temperament and came to the operation thoroughly scared, breathing 30 times a minute, pulse on systolic pressure only 100, diastolic 58. The ventilation of 13000 c.c. per minute had so reduced the CO_2 that the patient was already on the way to shock before the operation had begun, and this tendency was further increased for the first 15 minutes, but by rebreathing 400 c.c. of each breath, beginning this large rebreathing on the 10 minute line, the heart rate became slower progressively, while the blood pressures increased to their normal by the end of the operation. This patient actually left the table in better condition than when she came on, and remained so, as shown by the pulse and pressures at 2 o'clock and again the next day.

The notch in the diastolic pressure was caused by rough handling in exploring the abdomen at the 45 minute line. It was followed immediately by a fall in the systolic pressure and a rise in the pulse rate but as soon as the cause was discontinued, the pulse and pressures began to recover, showing that the shock-producing-influence had not been so prolonged as to exhaust the cardio-arteriole musculature.

ing and more gradual in its onset. The fall under chloroform is usually noticeable by the end of 15 minutes and within a few minutes

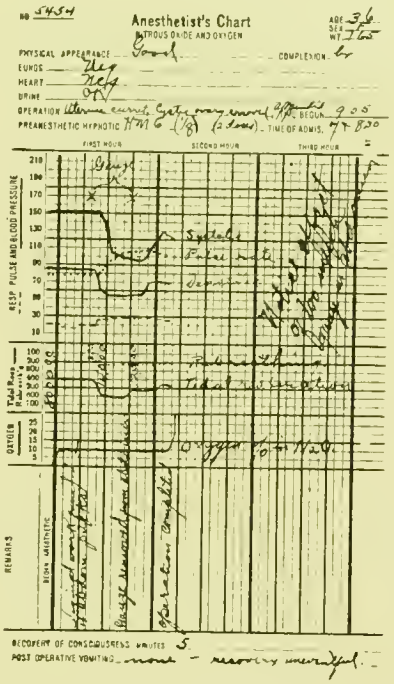
as pointed out by Fairlie, the low figures due directly to the anesthetic, are reached, when other factors may further decrease the pressures. The fall of ether does not usually begin under 20 minutes when properly administered, but the low figures may not be reached even during the operation, since there is often a tendency for the pressures to progressively fall after the patient has been returned to bed.



Case No. 5051. This case shows the effect on blood pressure of a brisk but short hemorrhage from the renal artery. The ligature accidentally slipped, but without any serious consequences to the patient.

The morphin-hyoscin-nitrous oxid-oxygen combination (without the use of ether) differs widely from either chloroform or ether, and deserves a few words of explanation. It has been erroneously claimed that nitrous oxid-oxygen increases blood pressure; at least this is not true clinically. However, these gases may be administered in any operation which is comparatively free of other shock-producing factors, for 2 hours without a material change in either diastolic or systolic pressure, but there is a time limit beyond which the blood pressures will progressively fall even under nitrous oxid-oxygen, but, differing from ether, this fall is discontinued at once upon removing the anesthetic and is followed by a comparatively rapid rise approaching the normal pressures within a few minutes. This data has been obtained by the writer during prolonged administrations for the relief of gall stone colic and eclamptic seizures.

The morphin and hyoscin which is almost universally used prior to nitrous oxid-oxygen, occasionally sets the pressures at from 5 to 15 mm. lower than the patient's normal, which is especially noticeable when the patient's normal pressures are abnormally high for the age,

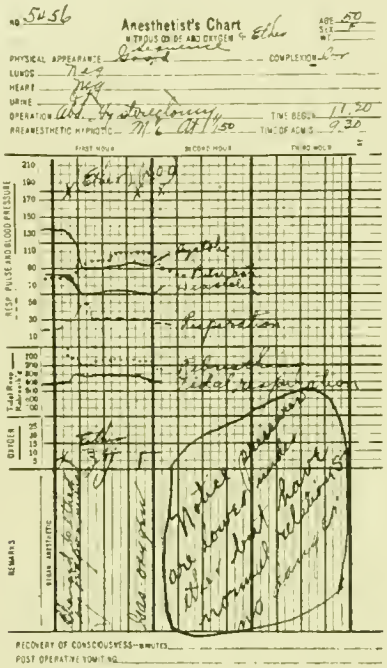


Case No. 5454. This chart shows the well-marked effect of four large abdominal pads or packs upon blood pressures, pulse and respiration. Too large an area of peritoneum was irritated. Notice the diastolic drop, followed at once by the pulse pressure. The rise in pulse rate was not marked, but noticeable. The pulmonary ventilation was increased. In ten minutes after the gauze was removed the patient's condition began to improve. While this trauma was not serious, it shows that a vicious circle would have been inaugurated had the gauze remained an hour longer. This effect on blood pressure would not have been detected by feeling the pulse, only the sphygmomanometer would show it.

but if administered in proper dosage they are of material assistance in relieving anxiety and the circulatory depression associated with it, as well as further assisting the general anes-

thetic in preventing shock in a severe or prolonged operation.

The three most important factors for comparison are: (1) the pulse pressure; (2) the diastolic pressure, and (3) the pulse rate.



Case No. 5456. This is a nitrous oxid-ether sequence case illustrating the frequent observation of the depressing action of ether on the heart muscle, causing a fall in blood pressure out of all proportion to the decrease in diastolic pressure. Nitrous oxid-oxygen was again used toward the end of the operation, but at no time was the patient in any danger.

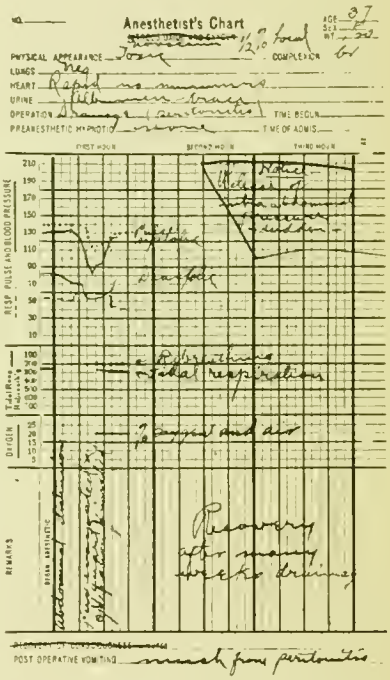
Each, of course, is influenced by the other. Under normal conditions an increase in the pulse up to a certain rate will elevate the diastolic and pulse pressures. A fall in pulse rate will produce an opposite effect. The pulse pressure represents roughly the immediate contraction power of the heart, while the diastolic pressure is a gross measure of arterial tonus.

SHOCK AND BLOOD PRESSURES.

In the discussion of blood pressure during operations shock necessarily occupies an important place. When it is appreciated that shock is not an instantaneous result of some surgical insult, but is a fairly slow and progressive change, characterized by inefficient circulation corresponding to changes in the pulse, respiration and blood pressures, which are readily studied, sphygmomanometric readings in the operating room as a means of diagnosis and prognosis should be established without question or delay.

UNNECESSARY PROCEDURES.

Many patients die daily of shock who might be saved by doing the operation in two steps, or by eliminating some unnecessary procedure, if it were definitely known that shock was coming on. The appendix is often removed while



Case No. .... This case was an abdominal drainage under ½ per cent. novocain. When the pus escaped collapse was so marked that for a few minutes death seemed inevitable. The respirations were so hurried that it was thought advisable to administer 20 per cent. oxygen with air, rebreathing 75 per cent. of each exhalation. Whether or not this patient would have recovered, unless resuscitated, it is difficult to state, but at any rate during this treatment the blood pressures rose quite rapidly, the pupils contracted and took on a regular outline, and the patient rallied. Similar cases of collapse have occurred under local anesthesia a number of times under my personal observation.

the abdomen is open for other surgery, because it is convenient and may save the patient future trouble. This little unnecessary manip-

ulation and waste of valuable time in a patient already in shock, not only occasionally, but frequently is the *last straw* in establishing the vicious circle of shock and heart fatigue which results in the death of the patient within three days.

UNRELIABILITY OF THE PULSE.

Shock or cardiovascular depression cannot be detected early by either counting the pulse, or palpating the radial artery. Frequent comparison by palpation with the view of detecting changes in the pressures by this method is practically useless in the hands of the most expert. A low diastolic pressure with a comparatively large pulse pressure generally feels like a good pulse, especially if the pulse rate is between 100 or 110, yet the sphygmomanometer will give the accurate information which is required for the interpretation of the patient's circulatory state.

Blood pressures are changing constantly from minute to minute, but this change should ordinarily not exceed a 10 per cent. variation, figured on the mm. of mercury pressure, without being regarded as abnormal. The pressures, however, may fall momentarily, such as in fainting, and yet even when the fall is great, unless it is sustained for some minutes is not attributable to shock, and is not accompanied or followed by any serious consequences, barring hemorrhage and absolute overdosage with ether or chloroform.

RELATION OF PULSE AND PRESSURES.

Shock is indicated when the pulse increases and the blood pressures either remain constant or fall. No serious case of shock occurs without low pressures, the heart rate is *usually* increased although not invariably so. It may be indicated also by a fall in pulse rate, which is accompanied by a marked decrease in pulse and diastolic pressures. The degree of shock is thus interpreted from a combination of the fundamental elements which would indicate various degrees of inefficiency in circulation.

CAUSES OF LOWERED PRESSURES.

In locating the cause of the shock it should be understood that the results come on frequently from 5 to 20 minutes after the cause; for instance, the most common cause of shock in the operating room is due to the introduction into the abdomen of a number of walling off packs so placed as to come into contact with a large distribution of peritoneal surface. The fall in the diastolic pressure is usually noticed to begin within 10 minutes, followed immediately, in most cases, by an increase in the pulse rate. This increase in pulse rate may be sufficient to carry the diastolic pressure up nearly to its normal point, the pulse pressure remaining fairly constant for a few minutes. Further irritation, oozing, or overdosing with the anesthetic, which is the second common cause of shock, reduces the pulse pressure, further increases the pulse rate while the inefficient heart is no longer able to compensate for the progressively dilating arterioles in the abdominal area, and the diastolic pressure gradually reaches such low figures as 60 or less mm. of mercury; the pulse pressure at that time being about 20 mm.

This is the picture of a typical case of shock, which if the operation could now be finished, and the causes removed would result favorably. But when such low pressures are reached, associated with pulse rates above 120 in a patient who, previous to operation, presented fairly normal pulse and diastolic pressures, there remains but half an hour until the vicious circle, previously referred to, will be established, unless some successful treatment is instituted or the cause removed. After the half hour of sustained low pressures and rapid pulse has been passed, almost every patient finally succumbs either shortly or within 3 days of surgical shock and heart exhaustion.

Upon opening the abdomen the intestines are pink, the smallest pulsating arteries visible to the naked eye may be noted. After irritating the peritoneum with gauze, exposure and handling, as is commonly done in abdominal surgery, and while the diastolic blood pressure is falling, a great many arterioles previously invisible, are now seen to pulsate showing positively that the marked congestion is due to a dilitation of these arterioles. Under such circumstances the intestine, which is also controlled by smooth muscle, is almost never seen to contract. It is not unlikely that a

weakened pulse pressure under such conditions contributes to the further widening of the arterial bed by the lack of proper mechanical (pulse) stimulus, or, to overstimulation if the pulse impact is too rapid. The volume of carbon dioxid adrenalin, ionizable salts, and oxygen, in the blood, probably all play a part in the balance between perpherial resistance and cardiac contraction. It is to be hoped that the surgeon in the near future will eliminate *dry bleeding* as effectively as hemorrhage is now controlled. But until that time, shock will continue to be a large factor in postoperative morbidity and mortality.

TRY YOUR HARDEST, GIVE ALL YOU CAN, ACT BY THE INNER LIGHT AND STAND TRUE TO WHAT YOU KNOW, AND LET THE RESULT TAKE CARE OF ITSELF. YOU WILL BE SURPRISED TO FIND THAT IT WAS NOT NEARLY SO BAD AS YOU THINK; PERHAPS IT WAS MORE THAN PASSABLY GOOD; POSSIBLY IT WAS EXCELLENT. IF YOU ARE TOO ANXIOUS ABOUT THE IMPRESSION YOU ARE LESS LIKELY TO SUCCEED THAN IF YOU ARE PASSIONATELY ENGROSSED IN WHAT YOU DO. ALL IS FORGIVEN TO SINCERITY.

WE ARE ALL WEIGHED DOWN NOW AND THEN BY THE SENSE OF THE DISCREPANCY BETWEEN WHAT WE MEANT TO DO AND WHAT WE DID. WE HOPED TO SAY THE WORD THAT WOULD GO TO THE SPOT, AND WE FLOUNDERED AND COULD NOT GET IT.

MANY A MAN BURNS WITH THE SENSE OF HIS RIGHT TO THE ATTENTION AND THE MONEY OF THE MORE PROSPEROUS; BUT A PURBLIND GENERATION PASSES BY ON THE OTHER SIDE IGNORING HIM. LET HIM BE PATIENT AND NOT LOWER HIS STANDARDS, AND IN TIME THE WORLD WILL CLIMB TO HIS LEVEL AND FIND HIM THERE, IF HE IS WORTHY.

—*Philadelphia Public Ledger.*

THE MODERN CONCEPTION OF RESPIRATION IN RELATION TO ACAPNIA, APNEA AND ANOXHEMIA UNDER GENERAL ANESTHESIA . GENERAL CONSIDERATIONS . ACIDOSIS AND KETONOSIS . INTERNAL RESPIRATION AND MUSCULAR ENERGY . CIRCULATION . THE OXYGEN AND CARBON DIOXID CAPACITY OF THE BLOOD . DYNAMIC CONSTANTS . CARBON DIOXID TENSION . INTERACTIONS . PULMONARY RESPIRATION . CARBON DIOXID TENSION IN THE ALVEOLAR AIR . OVER-VENTILATION AND APNEA . ACAPNIA AND ANESTHESIA . MORPHIN . RE-BREATHING . THE CONSERVATION OF INTESTINAL PERISTALSIS . PROPHYLAXIS

BY YANDELL HENDERSON, Ph. D. *NEW HAVEN, CONNECTICUT*

RESPIRATION IS, WITH the possible exception of reproduction, the broadest function of life. To be understood even in outline it must be thought of not merely as *breathing,* but as the sum and interaction of all the processes involved in and depending on the exchange of gases between the living cells of the tissues of the body and the outside atmosphere. Thus only can the general conceptions of this great function which have developed during the past few years he applied intelligently to such disturbances of respiration as acapnia, apnea and anoxhemia as they occur under anesthesia.

GENERAL CONSIDERATIONS OF RESPIRATION.

It is convenient to consider the processes constituting respiration under four heads:

(1) Internal or tissue respiration.

(2) The circulation, including the activity of the heart, the volume of the blood flow, the capacity of the blood to hold oxygen and carbon dioxid in physico-chemical combination, and the variations in this capacity in health and disease.

(3) Pulmonary respiration, including the mechanics of the thoracic movements, and the physical processes involved in the diffusion of gases between the air and the blood in the lungs—possibly also some active processes of a secretory or oxidative character as yet incompletely defined.

(4) The regulation of breathing by the respiratory center, and the behavior of this center under the various chemical and nervous influences which the ever varying conditions of life bring to bear upon it.

Although the chief interest and the principal advances during the past few years have concerned the second and fourth of these factors—the blood gases and the regulation of breathing—the most important of the four is and must always be the first named: *tissue respiration.* And here also the standpoint has broadened and is now broadening.

Until recently tissue respiration was thought of almost wholly as the chemical processes accompanying the transformation of the energy of the organic materials of the tissues into heat and work; in other words as a sort of combustion. With this idea in mind various theories were propounded by which oxygen was supposed to be built up into some hypothetical explosive substance—to be suddenly discharged when a muscle is stimulated to contraction. It was indeed known that a muscle placed in nitrogen or hydrogen gas contracts on stimulation; that the muscle under such conditions develops a greater acidity and becomes more quickly fatigued than when oxygen is supplied; and that these acid substances are rapidly destroyed, that is, converted into carbon dioxid, when the asphyxiated muscle

is again supplied with oxygen. It was known also that some animals, such for example as ascaris, can live indefinitely, and maintain a considerable activity, in a medium entirely devoid of oxygen. It is only recently, however, that we are beginning to realize the true significance of these facts; namely, that the functions of respiration are not only to allow combustion and the liberation of energy, but also, and of equal importance, to prevent acidosis.

In particular the recent work of A. V. Hill[2] has shown that the increase of internal respiration incidental to muscular work, and a large part of the heat liberation, rather follow than accompany the contraction of the muscles. The absorption of oxygen during the relaxation of a muscle following a contraction (and this is doubtless true also of the heart) provides for the destruction of such substances as lactic acid, resulting from the chemical processes involved in the production of the mechanical energy. We know from other sources that when the intensity of a muscular exertion exceeds temporarily the capacity of the circulation to transport the oxygen necessary for the destruction of these acid substances, lactic acid appears in the blood and a temporary acidosis occurs—lactic acid even being excreted in the urine. Similarly it has been shown that under the reduced oxygen pressure of high altitudes acidosis develops and persists as long as the subject remains at the altitude.[3] The condition affects both the blood and the breathing in essentially the same manner as that form of acidosis which accompanies at least some forms of nephritis.[4] In fact in normal persons the adjustment of this complex function has been shown to be determined by the barometric pressure to which they are accustomed.[5]

ACIDOSIS AND KETONOSIS.

It is significant also of the part which internal respiration plays in the prevention of acidosis that diabetes mellitus may fairly be regarded as at least in part a disorder of internal respiration—an inability to burn sugar. Until recently indeed the term acidosis was scarcely applied to any other condition than that occurring in the severer grades and terminal stages of diabetes.

In this connection it may be pointed out, however, that the substances appearing in the blood in acute diabetes to which the term *acidosis* has long been applied, would really be more properly indicated by *ketonosis*. They consist in the presence in the blood of various abnormal incomplete combustion products—acetone, diacetic acid, and oxybutyric acid, substances which doubtless exert some injurious influences apart from their acid character, and some of which are indeed not acids. Theoretically at least this ketonosis is to be distinguished from acidosis, which is properly defined as consisting in the presence in the blood and tissues of an abnormally high concentration of hydrogen ions, dissociated from non-volatile and unneutralized acids.

It is noteworthy that the disturbances of internal respiration incidental to diabetes tend to produce both ketonosis and acidosis, while acidosis from other causes, for example that of renal origin, or that due to residence at a great altitude, occurs without ketonosis.

INTERNAL RESPIRATION AND MUSCULAR ENERGY.

As internal respiration is a process closely associated with the energy expenditure of the body, it is principally controlled by the motor nerves. Every muscular contraction involves a corresponding subsequent activity of internal respiration to restore the active tissues to the normal resting condition necessary for another contraction. The activity of internal respiration does not depend therefore upon the amount of oxygen supplied. From the excess which the blood normally affords the tissues absorb as much as they need. Increased oxygen supply does not augment the vital combustion. Few mistakes are commoner or lead one further astray than the assumption that because a forced draft of air, or air enriched with oxygen, causes a fire to blaze up more brightly, therefore an increase in the oxygen supply of the body must augment the vital combustion. Heat production, and the amount of internal respiration during rest, depend largely upon the tonus of the muscles, regulated (in a manner as to the details of which we have still much to learn) by the motor nerves.

THE ROLE OF THE CIRCULATION IN RESPIRATION.

On the other hand, if the blood supply is insufficient, the first and predominant effect in any tissue is the limitation which it places upon the gaseous exchange of its cells. Thus the writer has shown that the terminal stage of shock sets in when the volume of the circulation has decreased to a point at which the blood returns to the right heart completely or nearly completely exhausted of its supply of oxygen.[6] The result of the deficiency from which the tissues thus suffer is an acute acidosis soon terminating in death. Wiggers[7] has reported observations upon the condition following hemorrhage which probably indicate a similar development of acidosis.

Similarly it appears that the partial asphyxia induced by an insufficient oxygen supply to the lungs in unskillful anesthesia, and the prolonged subminimal breathing following anesthesia in a patient rendered extremely acapnic must bring about their untoward effects largely because of the insufficient supply of oxygen carried by the blood to the tissues.

Turning now to the part which the circulation plays in respiration, the first fact to be emphasized is that although the blood is an intermediary in all, or nearly all, of the vital exchanges of the body, there is no other exchange of such peremptory importance as that of the gases. Food and water may be shut off for days, the kidneys may be excised, one or another of the internal secretions eliminated, and death follows only after weeks, days, or, at the least, hours. But when the gaseous exchange is stopped death is a matter of minutes. In reality the circulation is the central and most essential mechanism in the gaseous exchange; much more important in this respect than the thoracic movements to which the term respiration is sometimes narrowly limited. It is noteworthy that disturbances of the circulation as a rule affect the patient in such fashion that he suffers subjectively from a feeling of inability to get his breath, rather than from any sensation referred to the heart itself. Air hunger is usually due to low arterial pressure and an insufficient volume of blood flow.

The amount of energy which the body is capable of expending in health and disease, and the limits which determine how far many abnormal processes can go before death is inevitable, depend upon the total volume of oxygen and CO_2 which the circulation is capable of transporting. This in turn depends upon the volume of the blood stream and the capacity of unit volume of the blood to transport gases. The volume of the blood stream is the product of the heart rate and the volume of the systolic discharge. Failure of the heart's activity therefore brings about death by terminating respiration, in the broad sense in which the term is here used. Under normal resting conditions it appears that the blood returns to the right heart containing from two-thirds to three-quarters as much oxygen as it has when it leaves the left heart. There is thus normally a margin or factor of safety in this respect of 200 to 300 per cent. As already pointed out, when in shock or after hemorrhage the circulation fails, the final stage sets in when the circulation has been reduced to the point at which the blood stream brings to the tissues less oxygen than they demand, and returns to the right heart completely exhausted of oxygen.

OXYGEN AND CARBON DIOXID CAPACITY OF THE BLOOD.

The capacity of the blood to hold oxygen depends upon different conditions from those which underlie the capacity to hold carbon dioxid. The former depends upon the hemoglobin, the latter upon the alkaline elements in the blood. The two processes are in the main distinct. The exchange in the lungs and tissues does not consist in the blood taking up or giving off one molecule of oxygen in place of one molecule of CO_2 and vice versa. The oxygen is carried by the corpuscles, and CO_2 chiefly by the serum. The oxygen exchange is ordinarily about 20 per cent. greater than that of CO_2, a fact usually expressed in the statement that the respiratory quotient (the amount of CO_2 exhaled divided by the amount of oxygen absorbed) is usually considerably below unity. This is due to the fact that some of the oxygen is consumed in the oxidation of elements other than carbon, for example hydrogen and sulphur. Thus the theoretical respiratory quotient when carbohydrates ($C_6H_{12}O_6$)

alone are being consumed is 1.0, while for fats, in which the intramolecular oxygen is insufficient to convert all of the hydrogen into water, it is 0.7.

DYNAMIC CONSTANTS—CARBON DIOXID AS A CONTROLLING FACTOR IN THE BALANCE OF ACIDS AND BASIC SUBSTANCES.

It is due to the applications of physical chemistry to physiology that we have come to realize that CO_2 is not merely a waste product to be excreted from the body as rapidly and completely as possible, but that it is on the contrary a dominant factor in the regulation of one of the essential constants of the normal organism. There is no concept of modern physiology more significant than that which teaches that health consists in the maintenance of such constants as temperature, osmotic pressure, arterial pressure, the water constant or weight of the body, sugar constant of the blood, and other components and properties of the blood and lymph. These are dynamic, not static constants. They are of altogether different nature from such static constants as height, length of arm or color of eye. Each dynamic constant is the resultant of many factors in continual variation. The vegetative mechanisms of the body find their chief function in the compensating efforts by which these ever varying dynamic equilibria are balanced within such narrow limits of variation that health, which is their sum, is maintained.

The constant in which CO_2 plays the controlling role is the balance of acid and basic substances in the tissues and fluids of the body. As the matter is now thought of by physical chemists, pure water is neutral because the small part of it which is iodized, that is broken up into hydrogen atoms and hydroxyl groups, affords the same number of positively charged hydrogen ions and negatively charged hydroxyl ions. In any solution of any acid, for example a solution of hydrochloric acid, the acidity is due to the fact that in the dissociation the hydrogen ions are increased, and the hydroxyl ions diminished. In an alkaline solution on the contrary, for example one of NaOH, the hydroxyl ions exceed those of hydrogen. When a hydrochloric acid solution is neutralized with one of sodium hydroxid, the production of neutrality is not now thought of as consisting merely in the formation of the neutral sodium chlorid, but rather in the balancing of the hydrogen against the hydroxyl ions. Neurality is in other words such a balance of these ions as exists in pure water.

The slightest degree of acidity is peculiarly toxic for living protoplasm. Yet, as already shown, activity may produce acids in considerable quantity, while some foods and waters contain much alkali. Thus an autointoxication and acidosis, or alkalosis, would easily and frequently occur, were it not that the fluids of the body are provided with a system of dissolved substances which has a remarkable power of absorbing both acids and alkalis and maintaining approximate neutrality, and that the urinary and respiratory mechanism constantly effect compensations which prevent overstrain upon this system.

In this system as L. J. Henderson[8] has shown the principal elements are (1) the proteins, which are able to combine with alkalis and yet when free have so weak an acid character as to be without toxic effect; (2) the phosphates, which pass easily from the di-hydrogen to the di-sodium form, and vice versa, one weakly acid and the other weakly alkaline; and (3) particularly sodium bicarbonate and carbon dioxid. The regulation of the phosphates and alkalis of the blood is affected mainly by the kidneys, and is expressed in the well known variations in the relative amounts of the various urinary constituents and in the reaction of the fluid excreted.

CARBON DIOXID TENSION.

The finer and more immediate adjustments are made by the respiratory mechanism. It maintains the carbonic acid content of the blood at amounts such that this exceedingly weak acid balance, the weakly basic sodium bicarbonate, and the normal hydrogen ion concentration results. In health it appears that 55 to 60 volumes per cent. of carbon dioxid are present in the blood. Of this about 1 part in 20 is in the form of carbonic acid, the rest being held as sodium bicarbonate.[9] As we shall see, the respiratory center responds with extraordinary delicacy to the hydrogen ion concentration of the blood. By an increase or

decrease in the pulmonary ventilation the carbon dioxid is maintained at a tension such that the amount of carbonic acid in the blood, and with it the hydrogen ion concentration, is regulated to limits of variation narrower than any indicator, other than the respiratory center, as yet known to science can distinguish.

The transportation of oxygen in the blood is effected chiefly by the hemoglobin of the corpuscles, a substance which combines with and separates from oxygen in a peculiar dependence upon the partial pressure of this gas. This property is best expressed by what is termed the oxyhemoglobin dissociation curve, in which the abscissae express the oxygen tension or partial pressure—that is the pressure of this gas alone—and the ordinates show the amount of oxygen which the blood holds at the various pressures.

From the curves in Chart I it is evident that when the oxygen in the air of the lungs exceeds about 16 per cent. of an atmosphere (80 on the lower scale in the chart) the blood will take 95 per cent. or more of all the oxygen that the hemoglobin is capable of holding; it will be practically saturated. As the volume of ordinary breathing is such that the air in the alveoli contains about 4 or 5 parts of oxygen per hundred less than the inspired air—(16 or 17 per cent. as against 21 per cent.)—it follows that so long as the inspired air affords more than 16 per cent. of an atmosphere of oxygen, (760 mm. x. 16-121 mm. oxygen), the hemoglobin leaves the lungs with its hemoglobin practically saturated with oxygen. In blood containing the number of corpuscles and amount of hemoglobin normal for sea level, the oxygen saturation comes to about 18.5 volumes per cent.—that is, 100 c.c. of blood holds 18.5 c.c. of oxygen measured at 760 mm. of mercury and 0°C. Inhaling an atmosphere richer in oxygen can increase this amount by only the slight additional part which goes into solution in the plasma. An increase of pressure, as by insufflating into the lungs at a pressure higher than that round about the body, will impede the circulation mechanically, or even cause death by opposing the return of blood to the right heart, at a pressure much below any level that can materially increase the oxygen content of the blood.

From the dissociation curve it is also clear that as the venous blood returns to the right heart two-thirds saturated—at least during normal bodily rest—the tension of the oxygen in the tissues cannot be much below the pressure corresponding to this degree of saturation in the curve. For the tissues to take more oxygen from the blood, the tension in the tissues must fall lower. Otherwise the oxygen will not leave the hemoglobin. On general grounds it appears likely that the lower the oxygen tension falls the greater the chance that some incomplete combustion products may escape into the blood, or that in some other fashion a chronic acidosis may be established. This occurs both in normal men at great altitudes and in persons with cardiac disease and a subnormal circulation. It is noteworthy, however that influences of this sort are in large part compensated by a stimulation of the hematopoietic tissues, and particularly the bone marrow, to an increased production of red corpuscles.[3]

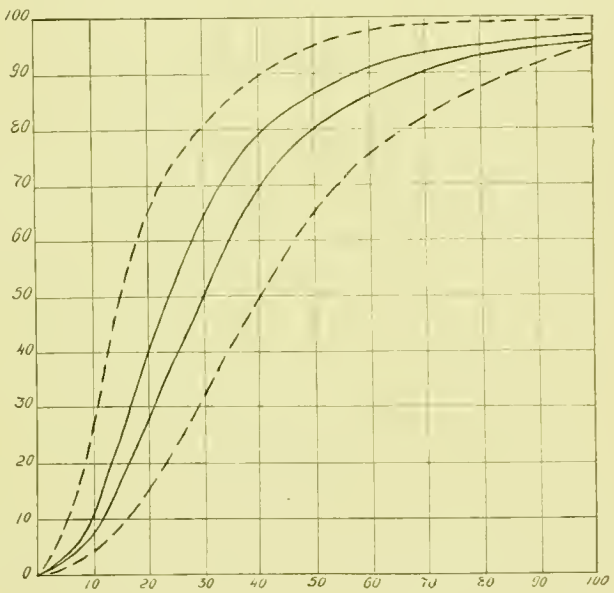


Chart 1. Oxyhemoglobin Dissociation Curves.

OXY-HEMOGLOBIN DISSOCIATION CURVES.

The two solid lines indicate the limits of variation in normal persons (Barcroft). The upper dotted line shows the characteristic displacement in extreme pleionexy, acapnia or alkalosis, and the lower dotted line that in in-

tense meionexy, or acidosis. Ordinates indicate percentage saturation—complete saturation being for normal persons 18.5 c.c. of oxygen for 100 c.c. of blood. Abscissae indicate the gas mixtures with which the blood would be in equilibrium at the various percentage saturations—100 on the scale corresponding to ordinary air at normal barometric pressure (760 mm.), i. e., 21 per cent. oxygen or 159 mm.

INTERACTION OF OXYGEN AND CARBON DIOXID TENSIONS.

The foregoing description of the transportation of CO_2 and oxygen as independent functions is not, however, entirely correct. It has been found that each gas exerts a small but significant influence upon the capacity of the blood to hold the other. In the presence of a high tension of oxygen, as in the lungs in comparison with the tissues, CO_2 is somewhat more readily given off, and this is of manifest advantage. Similarly the affinity of hemoglobin for oxygen is influenced by the amount of CO_2 and other acid elements in the blood. When, as in the lungs, the CO_2 content of the blood is lowered, the readiness with which hemoglobin takes up oxygen is slightly increased; while in the tissues, where the blood is exposed to a higher pressure of CO_2, the oxygen is more readily given off. This property is not confined to CO_2 and its dissolved form, carbonic acid, but depends apparently upon the hydrogen ion concentration of the plasma. It has been used recently, particularly by Barcroft[10] and his collaborators, as a means of determining the degree of acidosis in certain forms of cardiac and renal diseases. In the terminology adopted by Barcroft *meionectic* is the adjective applied to blood in which the affinity for oxygen is slightly decreased because of a high content of non-volatile acids. *Pleionetic* indicates a blood in which the affinity of hemoglobin for oxygen, even at relatively low pressures, is unusually great because of a low content of non-volatile acids in the plasma. Normal blood is said to be *mesectic*. Evidently *meionexy* is merely another name for acidosis. It signifies a shifting of the oxyhemoglobin dissociation curve to the left, as pleionexy indicates a shifting to the right. (See curves in Chart I.)

It should, however, be kept clearly in mind that in a person with a moderate degree of acidosis or meionexy the blood as it actually circulates in the body has not an appreciably higher hydrogen ion concentration—that it, it is not appreciably more acid—than in a normal individual. All that is true is that the non-volatile acids are abnormally high, or the alkalis are abnormally low, and that as a consequence the respiratory center automatically maintains a ventilation which keeps the carbon dioxid tension in the air of the lungs, and the carbonic acid tension in the blood, abnormally low. The lowering of that part of the hydrogen ion concentration which is due to carbonic part due to non-volatile acids. But the buffer action of the system, that is, its power to maintain neutrality against the addition of non-volatile acids, is diminished.

PULMONARY RESPIRATION.

Turning now to the topic of pulmonary respiration, the first point to be emphasized is the distinction between the volume of air breathed and the alveolar ventilation. This depends upon the existence of the respiratory dead space:[11] the mouth, nostrils, pharynx, larynx, trachea, bronchi and bronchioles. When in normal breathing an inspiration is drawn only about 60 to 80 per cent. of the air reaches the lungs themselves. The other 20 to 40 per cent. remains in the dead space, and takes no considerable part in the gaseous exchanges between the air and the blood. Accordingly the expired air consists of a varying amount, according to the amplitude of the breathing, of air from the pulmonary alveoli mixed with the air from the dead space. It is only the alveolar air which is included in the true pulmonary ventilation.

Even during the deepest possible expiration the lungs are not entirely collapsed, but still contain from 1,000 to 2,000 c.c. of air, while in ordinary normal expiration the so-called stationary air of the lungs probably amounts in a man of ordinary size to 3,000 c.c. or more. Thus when an inspiration of 500 c.c. is drawn, only about 350 c.c. of fresh air mixes with the stationary alveolar air, the other 150 c.c.

not passing beyond the dead space. When an expiration of 500 c.c. occurs only 350 c.c. of the pulmonary air is expelled along with the unaltered air of the dead space, leaving the trachea and mouth filled with pulmonary air.

It is clear that this fractional renewal of the pulmonary air tends to prevent the composition of the latter from being suddenly and greatly altered, as would be the case if there were no dead space, and the lungs were completely emptied and refilled with entirely fresh air at each breath. While atmospheric air contains approximately 21 per cent. of oxygen and only a neglible trace of CO_2, the alveolar air constantly contains, neglecting the water vapor, 5 or 6 per cent. of CO_2 and 14 to 16 per cent. of oxygen. It is this interior atmosphere with which the gases of the blood come into equilibrium, and by which through the influence of CO_2, the hydrogen ion concentration of the blood is maintained constant.

It would be a one-sided conception of respiration, however, to consider this function as exclusively under chemical control. In normal life breathing is influenced by countless nervous impulses. They come from the skin, from visceral organs, from the respiratory muscles, from the lungs themselves, and from the higher centers of the brain. Every syllable of spoken language is the result of a coordinated discharge from the higher intellectual centers through the centers controlling the muscles of respiration. Man is what he is intellectually, chiefly for two reasons: because he has hands, and (2) because he expresses himself, and thus learns to think, by speaking. It is the motor discharges through the respiratory mechanism which provide the symbols of abstract ideas which we term speech. In man respiration is a function on the border line between the vegetative or involuntary and the purely voluntary mechanisms. In animals respiration is almost wholly vegetative. Even in man it is peculiarly open to emotional influences—as weeping and laughter testify. Strong afferent influences, which appear in consciousness as pain, also induce the hyperpnea of suffering which we call crying, and increase the pulmonary ventilation far above that of the chemical regulation. Finally there are to be considered the normal afferent regulating nervous influences exerted by pulmonary branches of the vagi. These nerves are of great importance in reflexly inducing the change from inspiration to expiration and vice versa, the height of each phase and the need for reversal being notified to the respiratory center chiefly through these channels. As Scott[12] was shown, dissection of the vagi induces an ataxia of respiration.

In relation to the topics here under consideration the vagal influence is of importance chiefly in connection with the fact that even a slight positive pressure exerted in the lungs, as by intra-tracheal insufflation, exerts reflexly through the vagi an inhibitory influence from the respiratory center.[13] The center is thus rendered less sensitive to chemical stimulation. Its threshold is raised, so that a higher tension of carbon dioxid, or hydrogen ion concentration, is required to excite respiratory movements.

CARBON DIOXID TENSION IN THE ALVEOLAR AIR.

We return now to the chemical aspects of breathing. One of the most fundamental observations in modern physiology was the demonstration by Haldane and Priestley[14] that alveolar air is easily obtained. It is only necessary that the subject, breathing otherwise quite involuntarily, should make a sudden deep expiration through a piece of tubing so that a sample of the last of the air exhaled can be withdrawn for ayalysis from the end of the tube nearest the mouth. From analysis of the alveolar air it has been shown that for each individual there is a certain partial pressure of CO^2 in the alveolar air which is maintained within narrow limits of variation even under the most varied conditions. Thus during moderate physical exertion when the CO_2 production increases several fold above that occurring during bodily rest, it is found that the volume of the pulmonary ventilation is augmented in such close adjustment that the alveolar air CO_2 is only in very slight degree increased. It is also found that with increased, or within limits decreased, atmospheric pressure the volume of the pulmonary ventilation is automatically maintained at an amount so accurately adjusted to the CO^2 production of the body that the alveolar

CO^2 is maintained at the individuals normal partial pressure.

The same thing holds true when air enriched with oxygen or even when pure oxygen is breathed. Respiration is in fact within wide limits entirely uninfluenced by a high or low oxygen content in the pulmonary air, but continues to be regulated wholly, or almost wholly, according to the alveolar CO_2. If a man sitting still breathes 10 liters of air per minute, he continues to breathe 10 liters a minute even if pure oxygen is substituted for the ordinary air. As air is only about one-fifth oxygen, it is clear that if the oxygen needs of the body were in direct control of respiration he would need to breathe only one-fifth as much oxygen as air.

On the other hand the presence of even a small amount of carbon dioxid in the inspired air induces a distinctly measureable augmentation of breathing; as little as 3 to 4 per cent. may double the air breathed.[15] The regulation is so precise that as little 0.2 per cent. CO_2 above normal in the alveolar air doubles the pulmonary ventilation.[14]

When the oxygen content of the inspired air is reduced below normal, even by several per cent., respiration in most subjects continues for a time without noticeable alteration. It is only when the oxygen supply is decidedly deficient, and in some individuals not immediately even then, that the acidosis which results adds its influence to that of the CO_2 to excite respiration, and lowers the alveolar CO_2,[16] Under all ordinary circumstances as Miescher[17] many years ago expressed it, "carbon dioxid spreads its protecting wings over the oxygen supply of the body."

All the information available indicates that the control of the movements of the thorax and diaphragm, by which the pulmonary ventilation is effected, is localized in the so-called respiratory center in the medulla oblongata. It is here that, mainly at least, the hydrogen ion concentration of the blood exerts its regulative influence. This was shown most clearly by Fredericq[18] in his celebrated crossed circulation experiment. In this experiment the carotids of two rabbits are so connected with each other that the head of each animal receives its blood from the circulation of the other. Under these conditions the inspiration of a high percentage of CO_2 by one animal has no appreciable effect upon its own respiration, but excites marked hyperpnea in the other, whose respiratory center is reached by the blood in which the hydrogen ion concentration has thus been increased. Similarly an excessive artificial respiration administered to one of the animals so connected does not cause this rabbit to stop spontaneous respiratory movements, but does induce apnea in the other, whose head alone receives the acapnial blood.

OVER-VENTILATION AND APNEA.

Following up such experiments as this investigators in recent years, and especially Haldane and his collaborators, have shown that in the normal human subject a voluntary augmentation of respiration, which over-ventilates the blood and reduces its content of CO_2 is followed automatically by a period of apnea or at least of subnormal breathing. This condition lasts until the CO_2 content of the blood and pulmonary air has reaccumulated up to the threshold stimulating value of the respiratory center. If, however, as the writer[19] has shown, the forced breathing is done with a bag held over the nose and mouth, so that the washing out of CO_2 is prevented by a partial rebreathing of the expired air, no apnea follows. If no rebreathing is provided and the period of forced respiration is prolonged for several minutes, the subsequent apnea may continue until the oxygen in the blood and in the pulmonary air is in great part exhausted. The subject may thus become and continue for a time markedly cyanotic before the impulse to breathe returns with the reaccumulation of CO_2.[20]

In most persons a prolonged apnea of this sort is followed by a period of Cheyne-Stokes breathing. This fact, first demonstrated by Douglas and Haldane,[15] was shown by them to be due to the development of incomplete combustion products (lactic acid) because of the deficiency of oxygen. Owing to this acidosis a normal hydrogen ion concentration in the blood occurs with less than the normal amount of CO_2. Respiration is thus initiated. With the access of a fresh supply of oxygen, however, the acidosis is partly overcome; and as the CO_2 is still subnormal, another period

of apnea is induced. This alternation of apneas and short periods of breathing continues in lessening degree until the normal equilibrium of oxygen supply, and carbon dioxid production and elimination, is again attained

ACAPNIA AND ANESTHESIA.

To the condition of diminished carbon dioxid in the blood induced by excessive pulmonary ventilation, the term acapnia (from the Greek kapnos-smoke) is applied. Literally acapnia means smokelessness. As regards the hydrogen ion concentration of the blood, it is theoretically to be expected that acapnia would be equivalent to an alkalosis: a relative excess of hydroxly ions over hydrogen ions, due to a relative excess of alkaline over acid elements in the blood. On this point, however, there is as yet little information; and there are some facts which indicate that carbon dioxid, or more properly the carbonic acid ion, exerts specific influences in the body.

The initial stage of ether anesthesia, the so-called stage of excitement, usually involves a considerable amount of hyperpnea. The threshold of the respiratory center is lowered: that is, the center is rendered more excitable, and the excessive pulmonary ventilation produces a corresponding degree of acapnia. On the other hand, when full anesthesia is attained with ether, the threshold is restored to a normal level—a sensitiveness such that the carbon dioxid remaining in the blood is insufficient to induce breathing. Under full anesthesia with chloroform the threshold is elevated considerably above the normal level. In other words, under the latter condition the sensitiveness of the respiratory center is so much reduced that more than the normal amount of carbon dioxid is needed to excite the respiration to activity. In a long series of experiments, especially upon dogs, the writer found that by first maintaining the stage of ether excitement for a considerable time, and then inducing full anesthesia, apnea could almost invariably be induced. In extreme cases it was found that this failure of respiration continued until the deficiency of oxygen was so great that after about 8 minutes, the heart also failed and death resulted.[19]

This is the common form of failure of respiration under anesthesia.[22] Effects upon respiration similar to those of the stage of anesthetic excitement are also induced by pain. Suffering of any degree of acuteness induces excessive breathing. Anxiety and fear have a similar effect. The less resistant the subject the more excessive the pulmonary ventilation. Accordingly a more or less intense degree of acapnia is produced. When full anesthesia is administered to a patient who has suffered acutely it is therefore altogether in accord with theory that apnea—that is failure of respiration—should be liable to occur.[21]

MORPHIN AND ACAPNIA.

Among the drugs which tend to prevent the development of acapnia morphin takes first place. Even in ordinary dosage morphin has a tendency to elevate the threshold of the respiratory center to chemical stimulation, and thus to conserve the carbon dioxid store of the body.[22] Its principal value, however, lies in the protection which it affords the respiratory center from afferent stimulation, both such as comes directly from sense organs and such as comes indirectly through the higher conscious centers. A morphinized man or animal under powerful afferent stimulation or pain exhibits a relatively slight and brief hyperpnea as compared with an unmorphinized subject. The higher centers also are deadened and the exciting influence of anxiety and fear upon respiration is avoided. Most important of all, if the dose of morphin is sufficient and has been given a sufficient time beforehand, the exciting influence of ether during the induction of anesthesia is so far neutralized that full anesthesia is reached without the development of any considerable degree of acapnia. Less ether is needed to maintain anesthesia, and if the dosage of morphin is adequate there is an absolute prevention of the occurrence of the prolonged struggling, intense acapnia and subsequent nausea and gas pains characteristic of some so-called *bad subjects* when straight ether is used.

In addition to the use of morphin the most obvious procedure to counteract the exciting effects of ether and the development of acapnia is the rapid induction of full anesthesia with

as brief a period as possible in the stage of excitement. Thereafter uniformity of administration is the prime essential. *It cannot be overemphasized that failure of respiration is less often due to an excess of anesthetic immediately preceding the apnea than it is to some antecedent period or periods of insufficient etherization and hyperpnea with development of acapnia.*

is not only a measure of economy, and free from deleterious effects, but also that it exerts a marked influence in conserving the patient's vitality. At the same time the writer[24] showed by experiments on dogs and to some extent also on men that excessive pulmonary ventilation may so far deplete the body's store of carbon dioxid, and with it the vitality, as to induce a condition closely similar to the form of shock

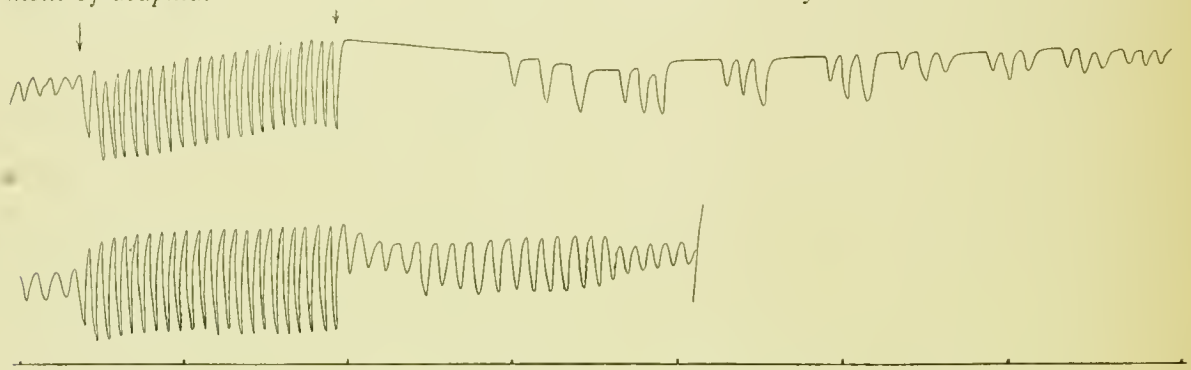


Chart II. Normal breathing followed by hyperpnea induced by inhaling ether.

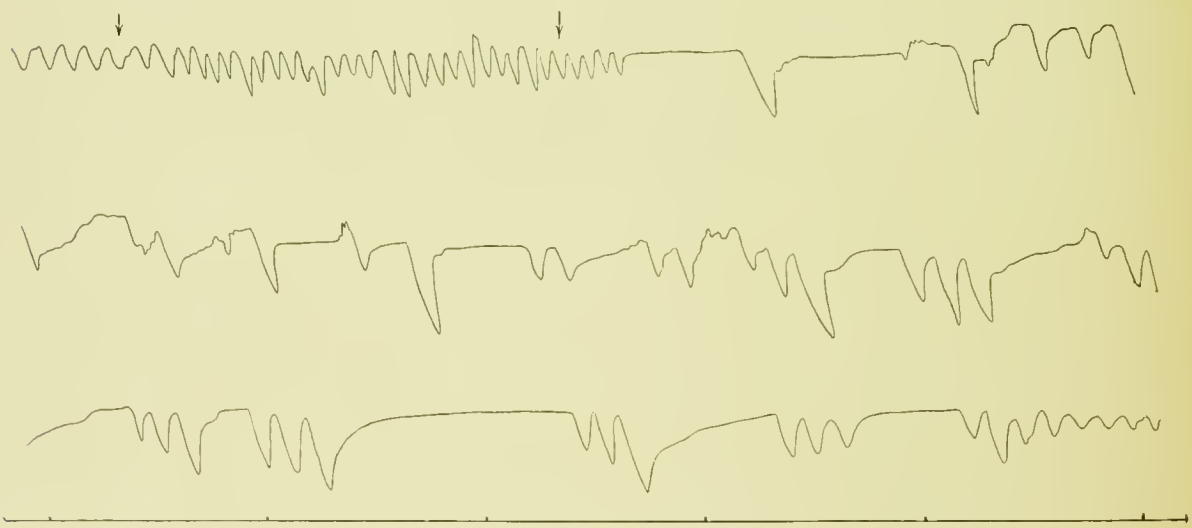


Chart III. Voluntary forced breathing. Upper curve without, lower curve with rebreathing.

REBREATHING AND OVER-VENTILATION.

In the past few years the practice of rebreathing as a preventive of excessive pulmonary ventilation has come into extensive use, and has been placed upon a firm scientific foundation. Gatch[23] was the first to show that in the administration of nitrous oxid, rebreathing

following hemorrhage. Parallel experiments in which the subject was made to rebreathe from a bag or through the enlarged dead space of a side tube demonstrated that an excessive loss of carbon dioxid could be prevented in this way, and that the prevention of acapnia served also to prevent the development of

shock. Hence acapnia is the cause of this form of shock.

In Charts II and III are reproduced tracings demonstrating the exciting influence of the initial stage of ether upon respiration and the decreased respiration which may follow, and also curves showing the effects of voluntary forced breathing and the neutralization of these effects by rebreathing into a bag.

Record of the respiration during an experiment in which the subject (Y. H.) inhaled through a mouthpiece and double valves from a bag of ether vapor of about 5.7 per cent., i. e. 5 c.c. of liquid ether volatilized in 20 liters of air. The ether had for some weeks been exposed to sunlight, and may have been more than ordinarily exciting on this account. The curve shows first normal breathing, then between the arrows the hyperpnea induced by inhaling the ether vapor, thereafter the respiratory disturbances which followed, and finally a return to normal breathing. The lower line indicates time in half minutes. (Chart II.)

Records of two experiments in which the subject (Y. H.) performed voluntarily forced breathing between the arrows. The upper curve shows the subsequent disturbance of breathing. The lower shows how these effects were prevented by the fact that in this experiment an excessive loss of CO_2 was prevented by rebreathing into a bag. Time record in half minutes. (Chart III.)

It must, of course, be understood that by rebreathing in connection with anesthesia is meant partial, not total, rebreathing of the expired breath. If air is used, there must be continually a sufficient exchange between that in the bag and that outside to keep the contents of the bag and alveolar air at an oxygen tension sufficient to allow the hemoglobin of the blood to take up practically a full charge of oxygen. Otherwise anoxhemia, cyanosis, and their evil effects will follow. Even when pure or nearly pure oxygen is administered the rebreathing cannot be complete for more than a few minutes at a time at most. Otherwise CO_2 accumulates in toxic amounts. Whatever the device or method employed, the extent of the rebreathing should be such as avoids any trace of cyanosis, while at the same time maintaining a full deep respiration. It should in all cases be sufficient to avoid that pallor which is, apart from failure of breathing, the most characteristic symptom of acapnia. As Bryant and the writer[25] have shown, the rule by which to regulate the amount of rebreathing is: *Keep the patient pink.*

ACAPNIA AND THE VENO-PRESSOR MECHANISM.

The pallor here referred to is perhaps the most interesting of the symptoms of acapnia. It is the first warning of a failing, or at least subnormal, circulation. From a long series of investigations the writer has been led to believe that this depression of the circulation is not primarily a failure of the heart, and that it is not due to a decreased tonus in the vasomotor nervous system. Apparently it is the effect of acapnia upon the *veno-pressor mechanism*—a factor in the circulation of great importance, but as yet incompletely defined nature. Under acapnia, as recent and as yet unpublished experiments by the writer indicate, the veins appear to contract and thus to decrease the return of blood to the right heart. It is this decreased venous return which accounts for the acapnial failure of the circulation under anesthesia or after intense pain, and the effects of hemorrhage. The full explanation of the matter is still to be sought. The broad facts as above stated may, however, be asserted now with a strong assurance of approximate correctness.

Observations of the writer as yet unpublished indicate that a marked increase in the flow to the right heart and amelioration of other acapnial effects can be induced by causing the subject to breathe air to which small amounts of CO_2 (4 to 6 per cent.) have been added.

REBREATHING, MORPHINIZATION AND PERISTALSIS.

Finally the influence of acapnia upon the stomach and intestines must be taken into account. Neither in patients during a laparotomy under the ordinary more or less acapnial methods of anesthesia, nor in animals under experiment with the abdomen opened without special precautions, is normal peristalsis seen once in a hundred, nor even in five hundred times. If, however, as the writer[26] has shown upon animals, the occurrence of acapnia is

prevented by means of morphin and rebreathing, and the viscera are protected from any considerable direct exhalation of carbon dioxid, entirely normal peristalsis may easily be seen in the stomach and in the large and small intestines. Exactly parallel results, as Bryant and the writer have pointed out, are obtained in patients under corresponding conditions in Rovsing's clinic, where a rebreathing method of etherization and adequate morphinization have been the routine method in thousands of cases during several years past.[25]

On the experimental side the work of Rona and Neukirch[27] has demonstrated that the carbonic ion is of critical importance in the maintenance of intestinal tonus and peristalsis.

The evidence on this matter is completed by the commonly observed fact that it is particularly the *bad subjects,* those who when etherized without morphin and without rebreathing undergo a prolonged period of excitement and excessive pulmonary ventilation, who later exhibit in corresponding intensity the gas pains which form one of the occasional, but none the less disagreeable and at times even dangerous, consequences of straight ether by an open method. As the acapnia theory comes to be more extensively understood and applied, such sequelae of unscientific methods will be regarded as reflecting upon the care and skill of the anesthetist in the same degree as the results of failure of asepsis now do upon the capacity of the surgeon.

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For additional references on this general topic see Bryant and Henderson, op. cit.

MORTALITY UNDER ANESTHETICS . DEATHS UNDER VARIOUS AGENTS AND METHODS . DIFFICULTIES IN COMPILING ACCURATE STATISTICS . RELATION OF ANESTHETIC MORTALITY AND POSTOPERATIVE COMPLICATIONS . DEATH RATES IN LARGE SERIES OF CASES . STATISTICAL TABLES . SURGICAL AND ANESTHETIC MORTALITY . CONCLUSIONS.

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WITHIN SIX MONTHS from the first demonstration of ether anesthesia, *two deaths* had been recorded from its use. Thomas Herbert died during an operation for stone under the 28 recorded administration of ether (Medical Gazette, March 5, 1847). Ann Parkinson failed to recover from the effects of ether, administered for the removal of a tumor of the thigh. (London Chemist, April, 1847, 167).

Neither time nor space permit chronicling the uninterrupted series of deaths under ether which have continued to occur up to the present time. The dangers attending the use of ether undoubtedly led Sir James Y. Simpson to experiment with chloroform. The death of Hannah Greener under chloroform on January 28, 1848, also put the stamp of danger on this anesthetic.[1] A committee appointed by the Royal Medical and Chirurgical Society in 1864 collected the reports of 109 chloroform fatalities which occurred between 1848 and 1865.[2] Kappeler recorded 101 deaths reported in the years 1865 to 1876.[3] Of the 210 chloroform deaths reported in these two collections of statistics, the period at which death occurred is stated in 75 instances. In 68, or 90 per cent. of these the patients died within the first 15 minutes of the administration. (See Cardiac Fibrillation and Chloroform Syncope, by A. Goodman Levy, herewith printed in the YEAR-BOOK.) Comte collected 232 deaths under chloroform. In 224 of these the period at which death occurred is mentioned, and in 112, or 50 per cent. of these, death took place before anesthesia was complete.[4] Hewitt found 130 chloroform deaths reported in the Lancet and British Medical Journal in the years 1880 to 1889. Of these 54 took place either before the operation or during some short or trivial operation.[5] (Anaesthetics, Hewitt:[1] 1912, 10:[2] 1901, 339:[3] 1901, 341:[4], [5] 1901, 3342.)

Neuber reported 71,052 cases of anesthesia with 24 deaths. 20,613 of these were chloroform cases with a mortality of 1 in 2,060; 11,859 were ether administrations with a mortality of 1 in 5,930. In 10,230 cases in which ether was preceded by chloroform the mortality was 1 in 3,410. (Muhsam: Med. Klinik, June 16, 1912.)

Flemming has analyzed 700 anesthetic fatalities, collected from reports of coroner's inquests in England during 3 years, 1910 to 1913. Chloroform was the anesthetic in 378 of these cases and mixtures containing chloroform in 100 more. In 223 cases death occurred before the operation was begun. (A Review of Inquests Concerning Deaths During Anesthesia, 1910-1913, A. L. Flemming: Proceedings of the Royal Society of Medicine, 1914, vii, Section of Anesthetics, 17).

The Committee of Anesthesia of the American Medical Association, in 1912, reported that: (1) the use of chloroform as an anesthetic for major operations is no longer justifiable; (2) for minor operations the use of chloroform should cease; (3) chloroform is sometimes found convenient for initiating anesthesia in alcoholics or other difficult subjects. (Journal Amer. Med. Association, June 15, 1912, 1909). The value of the first and second sweeping conclusions are manifest. In regard to the third, drawing our conclusion from the unanimity of the reports of the danger at-

tending the induction period of chloroform anesthesia, we are justified in stating that chloroform should never be used as a preliminary to other anesthetics.

Besides the deaths resulting immediately from chloroform a large number of fatalities due to delayed chloroform toxemia have been recorded.

TABLE I.

Deaths Due to Delayed Chloroform Poisoning

Reporter	Deaths	Reference
Tuffier	2	Presse Medicale, 1906, xiv, 309
Madison	2	Wisconsin Med. Jour., March, 1906
Stevens		Jour. Missouri St. Med. Asso., October, 1909
Haberlin		Corr. Blatt. f. Schw. Aertze, Nov. 1, 1910.
Muskens	2	Mitt. aus d. Gren. Med. u. Chir., xii, No. 4
McCowan) Fontaine)		Journal A. M. A., July 30, 1910.
Stiles	8	Journal A. M. A., February 10, 1912
Corner		Clinical Journal, May 22, 1912
Monroe	3	Journal A. M. A., January 13, 1912
Keil	10	Deut. med. Wochen. May 14, xi, No. 20
Ottow	15	St. Peters. med. Zeit. Sept. 14 xxxvii, No. 17 (Recorded from literature)
Fairlie		Lancet, December 19, 1914
Sipple	40	Archiv. f. Gynecol., 68, No. 1 (Recorded from literature)

Braun states that late chloroform fatalities present the picture of acute yellow atropy of the liver. (Centr. f. d. Gren. d. Med. u. Chir., Sept. 8, xvii, 1-3). Graham, attempting to solve the problem of delayed chloroform poisoning, attributes it to the hydrochloric acid action of the alkyl halids set free in the oxidation of chloroform in the tissues. (See Late Chloroform Poisoning, A. E. Graham, herewith printed in the YEAR-BOOK).

In the adenoid and tonsil operation, chloroform is especially fatal. Packard reports twenty-nine deaths from chloroform or ethyl chlorid during tonsillectomy. (Journal A. M. A., August 29, 1909). Chaldecott reported 50 deaths from chloroform during adenoid operations, 5 of them having taken place in the practice of experienced anesthetics. (Lancet, September 13, 1902). Chloroform was at one time believed to be free from danger when used in obstetrical cases. A number of fatalities from its use in labor have been reported. Hodgson records the case of a normal, healthy woman, who died under chloroform in an obstetrical case. (Atlantic Jour. Rec. of Med., November, 1911). Sitting recorded 5 deaths from chloroform in obstetrical cases in Iowa. (Journal A. M. A., February 1, 1908).

DEATHS UNDER ETHYL CHLORID.

Lotheissen reported the first death under ethyl chlorid anesthesia. (Muench. med. Woch., 1900, 18). McCardie collected reports of 8 deaths including that reported by Lotheissen. (Lancet, October 7, 1905). Luke recorded 8 additional deaths. (British Dental Jour., Nov. 1, 1905). McCardie collected 21 deaths, including those already referred to. He notes 9 other deaths that have occurred in the north of England, of which no details are available. (British Med. Jour., March 17, 1906). Lee reported 5 deaths at the Pennsylvania Hospital, of which one was solely due to the anesthetic. (Annals of Surgery, Nov. 1908, 641). Miller recorded 43 deaths under ethyl chlorid, of which at least 21 were due to the anesthetic. (Journal A. M. A., Nov. 23, 1912). Flemming reports 6 ethyl chlorid deaths, (Loc. cit).

DEATHS UNDER NITROUS OXID.

Hewitt was able to find only 30 deaths from nitrous oxid reported in the literature during a period of 40 years. 17 of these deaths were

TABLE II.

Deaths Under Nitrous Oxid-Oxygen Anesthesia.

Reporter	Deaths	Reference
Lydston	1	Medical Record, Nov. 12, 1910, 866
Crile	1	Southern Med. Jour., Jan. 1910, 29
Allen	3	Boston Med. & Surg. Jour., Oct. 19, 1911, 589
		Journal A. M. A., Feb. 10, 1912, 396
Gatch	3	Journal A. M. A., Nov. 11, 1911, 1593
Olow	1	Beit. zur. klin. Chir., Dec. 1911
Boys	1	Surg. Gyn. & Obst., April 1912, 388
Miller	1	Journal A. M. A., Nov. 23, 1912, 1847
Flagg	1	N. Y. St. Jour. Med., Nov., 1912
Teter	3	Journal A. M. A., Aug. 7, 1912, 1849
		Journal A. M. A., Nov. 23, 1912, 1872
Salzer	1	Journal A. M. A., Nov. 23, 1912, 1862
Buchanan	1	Journal A. M. A., Nov. 23, 1912, 1860
Babcock	2	Amer. Jour. Obst., May 1914, 844
Luke	1	New York Med. Jour., Jan. 30, 1915

In 11 of these cases death is reported as due to the anesthetic.

due entirely or in part to the anesthetic. (Anaesthetics: Hewitt, 1901, 228.) Deaths from nitrous oxid are reported occasionally, but rarely in proportion to the immense number of administrations. There are 12 nitrous oxid deaths in Flemming's list, (Loc. cit.) The following observers have reported a total of 21 deaths under nitrous oxid-oxygen anesthesia.

DEATHS UNDER LOCAL ANESTHESIA.

On account of the unshaken belief in the safcty of local anesthetics it is difficult to obtain reports of deaths from these agents. Fatalities, however, have been reported by such observers as Proskauer, (Ther. d. Gegenwart, Dec., liv, No. 12), Lichtenstein, who also refers to a case reported by Ritter, (Ibid, Feb. xvi, No. 2), Miller, (Journal A. M. A., Jan. 17, 1914, 196), Gwathmey, 2 cases, (Anesthesia, 1914, 844), and Flemming, 6 cases, (Loc. cit.)

DEATHS UNDER SPINAL ANESTHESIA.

Strauss collected 46 deaths resulting from spinal anesthesia. In 25 cocain was employed. In the remaining 21 cases only 3 deaths were due solely to the anesthetic. Chiene collected 22 deaths, of which very few were due to the anesthetic alone. Hardouin reported one death, but found 15 other in the literature. Violet and Fisher collected 30,000 cases of spinal anesthesia from the literature with 36 deaths, giving a mortality rate of 1 in 633.

TABLE III.

Deaths Under Spinal Anesthesia

Reporter	Deaths	Reference
Strauss	46	Deut. Zeit. f. Chir., July 1907, 275
Chiene	22	Brit. Med. Jour., Sept. 18, 1909, 788
Kohler	12	Deut. Zeit. f. Chir., 1909, 16
Hardouin	16	Archiv. gen. d. Chir., Aug. 25, 1908
Violet, Fisher	36	Lyons Chirurgical, Nov. 1910
Scandola, Merusal	2	Gaz. deg. osp. e del. clin. xxxvi
Reynolds		Amer. Jour. Obst., July, 1909, 78
Senge		Zeit. f. Geb. u. Gynecol., lxxiv., No. 2
Bainbridge		Journal A. M. A., Nov. 23, 1912
Page	2	Lancet, May 16, 1915
Rockey		Journal A. M. A., Feb. 8, 1913
Flemming	8	Proc. Roy. Soc., loc. cit.

FATALITIES UNDER SCOPOLAMIN.

Mass found 11 deaths from scopolamin in 1,449 cases, a mortality rate of 1 in 134. Therap Monat. Aug. 1905). DeMaurans collected 22 scopolamin deaths, (Semaine med., Nov. 8, 1905). Wood found 23 deaths, of which 9 were due solely to the anesthetic, (American Medicine, 1906, xvii 546). Deybert and Dupont reported 7 scopolamin deaths and collected 22 deaths from the literature, (Revue de Chir., June, 1910, xxx, 6). Hatcher states that about 30 fatalities have resulted from the use of scopolamin, (Journal A. M. A., Feb. 5, 1910, 447).

FATALITIES UNDER OTHER METHODS.

The mortality from anesthetic agents is modified by some of the methods of administration. In 16 cases of intravenous anesthesia. Pikin met with one death, (Weiner klin. Wochen, March 5, 1910). Homan and Hassler had but one fatality in 350 cases, (Annals of Surgery, December, 1913). Under intratracheal anesthesia Woolsey reported 5 deaths, (N. Y. State Med. Jour., April, 1912). Robinson found 7 deaths among 1402 cases, (Surg. Gyn. & Obst., March, 1913, 296).

Deaths under rectal anesthesia have been reported by Weir (Medical Record, May 3, 1884), Baum, 2 deaths, (Zeit. f. Chir., March 13, 1909); Carson, 2 deaths, (Interstate Med. Jour., May, 1909); and Cunningham, (Boston Med. & Surg. Jour., March 24, 1910).

Certain conclusions result naturally from a study of reported deaths under anesthetics: (1) that none of the anesthetic agents or methods are entirely free from danger; (2) that many deaths have resulted from the routine use of these agents, and (3) that some of these deaths were avoidable.

DIFFICULTIES ENCOUNTERED IN ATTEMPTING TO COMPILE ANESTHETIC MORTALITY STATISTICS.

To compile accurate statistics of mortality from anesthetics is a matter of great difficulty. It is impossible to determine accurately the total number of administrations. There is also no accepted standard by which we can determine what constitutes a death due to an

anesthetic. Roberts states that "death in general anesthesia is usually due to poisoning from incompetent administration." (Surg. Gyn. & Obst., August, 1911, 220). On the contrary Williams believes that the anesthetic deaths reported "are not always due to the anesthetic." (Clinical Journal, December 23, 1908). Most of the deaths under anesthetics are never reported at all in available form, (Ferguson: Journal A. M. A., Nov. 23 1912, 1860). In most instances it is impossible to compile accurate statistics of deaths from anesthetics from municipal records of deaths or from hospital records. Gwathmey was able to obtain reports from only 99 among 1,400 hospitals circularized in regard to anesthetic mortality, (Journal A. M. A., Nov. 23, 1912, 1844). In many instances, frequently unintentionally, anesthetic deaths are reported as due to other causes. Deaths from status lymphaticus have been frequently reported.

TABLE IV.

Anesthetic Deaths from Status Lymphaticus

Reporter	Deaths	Reference
Kundrat	10	Wein, klin. Woch., Jan. 3, 10, 17, 24, 1895
Rubra		Lancet, Dec. 21, 1907, 1759
Brown		
McCardie	30	British Med. Jour., Jan. 25, 1908, 196
Hilliard		Ibid, 202.
Roberts	17	California St. Jour. Med., Aug., 1908
Humphrey	5	Lancet, Dec. 26, 1908, 1870
Bradley		Journal A. M. A., liv., 1910, 1785
Howell	1	Journal A. M. A., Mar. 28, 1914, 1014
Emrys	3	Jour. Path. & Bact., April, xviii, No. 4, 683
Roberts		

Henderson believes that "*in the large majority of fatalities of the cardiac type, these three expressions,* (1) *hypersensibility to anesthetics,* (2) *heart disease, or* (3) *status lymphaticus, are mere excuses. The patient is killed by the method of anesthesia.*" (Surg. Gyn. & Obst., August, 1911, 161).

In many cases of death during or following operation, it is difficult or impossible to determine what influence the anesthetic has had in producing the fatality. In postoperative deaths due to peritonitis, septecemia, pulmonary, cardiac, cerebral embolism or hemorrhage, the influence of the anesthetic need not usually be considered. Among deaths due to suffocation from inspired vomitus, asphyxia from faulty position, tight bandages about the neck or pressure on the larynx during an operation, the anesthetic agent employed should not be blamed, although the fatality would not have occurred if no anesthetic had been administered. The anesthetic may contribute to the fatality in deaths reported as due to shock, pneumonia, nephritis, acid intoxication, endocarditis, or status lymphaticus. Deaths due entirely to the anesthetic occur as the result of overdosage or of improper administration. Henderson has called attention to the dangers attending the intermittent administration of anesthetic agents: "*It is not what the anesthetic agent does to the patient at the time of death, or five minutes before, which kills him. It is the treatment which the patient receives half an hour or an hour before which really causes the fatality.*" He concludes *that "In prolonged, light anesthesia and excitement, and especially in any intermittent method of administering ether or chloroform, peculiar dangers are involved.*" (Surg. Gyn. & Obst., August, 1911, 161).

RELATION OF ANESTHETIC MORTALITY AND POSTOPERATIVE COMPLICATIONS.

The study of mortality from anesthetics is incomplete without considering the role played by anesthetic agents in the production of postoperative complications which sometimes result fatally. In the production of postoperative pulmonary complications, nephritis, acid intoxication, cardiac, pulmonary or cerebral embolism, phlebitis, fat embolism, acute gastric dilatation, septic infection and in shock, the effect of the anesthetic agent is undetermined.

Ether anesthesia certainly diminishes the natural resistance to acute infections. Graham has found that : "*the reduction of the phagocytic power of the blood after an ordinary ether anesthesia continued in different experiments over periods of two days to several weeks in duration.*" (Journal A. M. A., March 26, 1910).

Ether anesthesia causes a marked decrease in the coagulation time of the blood, most marked from the seventh to the tenth day. This

may have an important bearing on the occurrence of embolism and thrombosis a week or ten days after anesthesia. Nitrous oxid, on the contrary, increases the coagulation time of the blood. (Hamburger and Ewing: Journal A. M. A., March 26, 1910).

Apperby found that the effect of ether anesthesia on the kidneys was negligible, but that chloroform injured the kidney cells to such an extent as to *"interfere very seriously with their chief means of excretion."* (British Medical Journal, Sept. 14, 1912). Seelig stated that: *"postoperative pneumonia is by no means solely referable to ether. Aspiration of mucous or vomitus, exposure and pulmonary embolism have been pretty clearly demonstrated to be the predisposing factors."* (Annals of Surgery, August, 1905). Wolf believes that postoperative pulmonary complications are due to a combination of factors; the chilling of the body, the aspiration of secretions, injury from the anesthetic and from displacement of organs by raising parts of the body. (Deut. Zeit. f. Chir., May, 1907). Homans divides postoperative complications into three classes: (1) those directly dependent upon the narcosis and resulting directly from the inhalation or aspiration of septic material into the lungs. (2) hypostatic pneumonia depending upon feebleness of the circulation and inability to keep the lungs clear, and (3) embolic cases. (Bulletin Johns Hopkins Hospital, April, 1909). Chapman recorded a series of experiments on the irritating effects of ether and concluded that: *"ether has a distinct irritating effect upon the lungs causing a swelling of the alveoli congestion of the alveolar tissue, and even intra-alveolar hemorrhage, which increases with the amount of forcing or crowding of the anesthetic."* (Annals of Surgery, 1904, xxxix, 700). Lawen found pulmonary complications as frequently under local as general anesthesia in the laparotomies performed at the Leipsic clinic. (Münchner med. Woch., Oct. 3, 1911). Mikulicz has shown that the percentage of acute pulmonary complications following operations is relatively greater in local anesthesia than if a general anesthetic is given. (Eisendrath: American Medicine, Nov. 15, 1903).

To obtain statistics of postoperative complications in a hospital, an elaborate cross reference system must be in use. Such systems have been installed in a number of institutions and detailed information concerning these complications is now rapidly accumulating. Homans has collected statistics of 15,043 laparotomies reported from German clinics with an average mortality due to lung complications of about 4.4 per cent. He found statistics of 3,089 laparotomies from Boston hospitals with a mortality of 0.4 per cent., from pulmonary complications. (Bulletin Johns Hopkins Hospital, April, 1909). Beckman recorded 6,825 operations with pulmonary complications in 87 cases, none of which resulted fatally. (Surg. Gyn. & Obst., May, 1914).

Skeel has contributed an exceedingly valuable article on the "Mortality of Abdominal Surgery." (Journal Mich. St. Med. Soc., Feb., 1915). He analyses a series of 1,032 cases, in which death occurred in 32 instances. He compares, *"surgical mortality, which may be defined as death in the hospital of any patient from any cause if that patient has been operated upon, and operative mortality, that is, death directly or indirectly as the result of operation, whether the disease for which operation was performed was necessarily fatal or not. Another factor quite as potent in its influence upon the apparent mortality as the basis upon which percentages are figured, has to do with the type of cases upon which any reporter is operating."* In Skeel's series there were eight operative deaths and five deaths from pneumonia. Of the latter cases, one died 21 days after operation, another after 29 days. "One death was from lobar pneumonia, which began eight hours after operation, in which nitrous oxid was the anesthetic. It seems certain that in this instance the pneumonia was a coincidence and not the result of ether operation or the anesthetic." Concerning anesthesia, Skeel concludes that: *"ether is safe so far as primary mortality is concerned, in the hands of a fairly competent anesthetist, if anesthesia is not so prolonged as to cause ether poisoning. Nitrous oxid is tolerated for a much longer time than ether, is the safest known general anesthetic in the hands of an expert, and the most dangerous of all general anesthetics when given by any other."*

REPORTED MORTALITY RATE FROM ANESTHETICS IN SERIES OF CASES.

It is customary to compute the rate of mortality under anesthetic agents from recorded series of administrations in which the anesthetic deaths are reported. Such statistics are of value in determining the comparative danger from the anesthetic agents employed. Records made from personal observation or from intimate knowledge are preferable for this purpose. The following series of ether and chloroform administrations have been reported:

TABLE V.

Mortality Rate Under Ether Anesthesia				Mortality Rate Under Chloroform			
Reporter	Cases	Deaths	Mortality Rate	Reference	Cases	Deaths	Rate
Richardson	8,431	1		Anesthetics: Hewitt, 1912, 138	35,162	11	1 in 3,196
Julliard	314,738	21	1 in 14,987	Ibid; 138	524,507	161	1 in 3,258
Ormsbee	92,815	4	1 in 23,204	Ibid; 138	152,260	53	1 in 2,837
St. Barth. Hospital	37,277	4	1 in 8,318	Ibid; 139	42,987	33	1 in 1,300
German Sur. Society	56,333	11	1 in 55,112	Eisendrath: American Med., November 15, 1902	240,806	116	1 in 2,075
Neuber	11,859	2	1 in 5,930	Muhsam Med. Klinik, June 16, 1912	20,613	10	1 in 2,061
Gwathmey	294,653	65	1 in 4,533	Anesthetics: 1914, 855	16,390	8	1 in 2,048
McGrath	49,057	0		Journal A. M. A., Oct. 25, 1913	1,300	0	
The average death rate from ether in this series is 1 in 8,010 cases				The average death rate from Chloroform in this series is 1 in 2,665			

W. H. Keen, of Philadelphia, has collected a series of 262,002 cases of ether administration with 34 deaths, showing a mortality rate of 1 in 7,705. (Boston Med. & Surg. Jour., Dec. 2, 1915).

Peterka collected 100,971 cases of ethyl chlorid anesthesia with 9 deaths, giving a mortality rate of 1 in 11,219. (Beit. z. klin. Chir., 1912, 81, 436); Miller collected 53,403 cases with 4 deaths due to the anesthetic, a mortality of 1 in 13,365; (Journal A. M. A., Nov. 23, 1912, 1847). The following series of cases of ethyl chlorid anesthesia are noteworthy.

1,500,000 cases of nitrous oxid anesthesia, with only 2 deaths, have been reported, (Birmingham Med. News, April, 1893); Buxton reports 1,001,000 cases with one death, (Anesthetics; 1900, 297), and Gwathmey estimates the death rate from nitrous oxid at 1 in

TABLE VI.

Deaths Under Ethyl Chlorid Anesthesia

Reporter	Cases	Deaths	Reference
Soullier	8,417	0	Bull. med .Paris, 1895, 417
Lotheissen	2,550	1	Ware: Med. Record, April 6, 1901
Newman	1,867	1	Cumston: Bost. Med. & Surg. Jour., January 1, 1905
McCardie	12,000	4	British Med. Jour., March 17, 1906
Luke	2,000	0	Lancet, May 5, 1906
Lee	5,575	1	Intern. Clinics, iv, 19th. Series
Herrenknecht	3,000	0	Muench. med. Woch., Dec. 3, 1907
Webster	1,880	0	Surg. Gyn. & Obst., April, 1909
Steida	1,000	0	Med. Klinik, March 24, 1912
Zanda			
Miller	6,648	1	Journal A. M. A., Nov. 23, 1912
Hornabrook	18,813	0	Aust. Med. Gaz., April 25, 1914
Greene	5,000	0	Amer. Jour. Surg., July, 1915
Ware	15,000	0	Amer. Jour. Surg., July, 1915

20,000, (Anesthetics, 1914, 844). The following series of nitrous oxid-oxygen anesthesias have been reported, (Table VII).

Among these 35,063 cases, there were 68 deaths, a mortality rate of 1 in 515. Strauss collected 22,717 records of spinal anesthesia

TABLE VII

Deaths Under Nitrous Oxid-Oxygen Anesthesia.

Reporter	Cases	Deaths	Reference
Gwathmey	8,585	0	Journal A. M. A., Nov. 23, 1912, 1845
Jones	13,000	1	Ohio St. Med. Jour., August, 1915
Lower, Crile	34,946	0	Anoci-Association: 1915, 245
Teter	23,952	1	Journal A. M. A., Nov. 23, 1912, 1849

Teter has collected 938,924 cases of nitrous oxid anesthesia: 32,172 cases of nitrous oxid and air, and 190,724 cases of nitrous oxid-oxygen anesthesia, a total of 1,161,820 cases with 2 deaths, (Dental Cosmos, Sept. 1915, 1028). Gwathmey collected reports of 14,878 cases of operations under local anesthesia with no deaths. (Journal A.M.A., Nov. 23, 1912, 1845).

The following series of cases under spinal anesthesia have been reported, (Table VIII).

with 46 deaths. Chiene collected 12,000 cases with 36 deaths, (Anesthesia: Gwathmey, 1914, 597; Lyons Chirurgicale, Nov., 1910); and the average death rate from these three series was 1 in 623.

H. C. Wood, Jr., collected from the literature, 1,988 cases of scopolamin anesthesia with 23 deaths. He carefully analyzed these and decided that the fatality in 9 cases was due to the anesthetic, giving a mortality rate of 1 in 221. The following series of cases of scop-

TABLE VIII.

Deaths Under Spinal Anesthesia

Reporter	Cases	Deaths	Reference
Risch	315	2	Zent. f. Gny., July 24, 1907
Chaput	7,000	0	Anesthesia: Gwathmey, 1914, 598
Krönig, Gauss	1,000	3	Muench. med. Woch., Oct. 7, 1907
Colombani	1,100	0	Wein. klin. Woch., Sept. 3, 1909
Gray	300	1	Anesthesia: Gwathmey, 1914, 598
Hohmeier	2,400	12	Archiv. f. klin. Chir., xciii, No. 1
Jonnesco	2,963	2	Bull. de l'Acad. de med., 1910
Violet, Fisher	270	1	Lyons Chir., November, 1910
Kohler	7,780	12	British Med. Jour., Jan. 15, 1910
Hahn	708	8	British Med. Jour., Jan. 15, 1910
Helm	1,419	0	Beit. z. Klin. Chir., lxxi-v
Barker	2,354	3	Anesthesia: Gwathmey, 1914, 589
Gwathmey	521	0	Journal A. M. A., Nov. 23, 1912, 1845
Bainbridge	1,065	1	Journal A. M. A., Nov. 23, 1912, 1855
Allen	320	0	Journal A. M. A., Nov. 23, 1912, 1841
Babcock	5,000	11	Amer. Jour. Obst., November, 1914
Gellhorn	63	0	Journal A. M. A., June 27, 1914
Merenes	169	0	Annals of Surgery, December, 1913

olamin anesthesia have also been reported. (Table IX).

TABLE IX.

Deaths Under Scopolamin Anesthesia

Reporter	Cases	Deaths	Reference
Maass	1,499	11	Therap. Monat. August, 1905
Roith	4,000	18	Muench. med. Woch., 1905, No. 46
Muhsam	28,809	5	Med. Klinik, June 16, 1912
Viron	2,000	25	Progres. Med., xxii, 1906, 97
Morel			
Beach	1,000	0	Amer. Jour. Obst., May, 1915
Rongy	2,000	0	Amer. Jour. Obst., Dec., 1915

The average death rate from scopolamin in these series is 1 in 666 cases.

In compiling these statistics of the mortality rate of various anesthetics, not all available figures have been included. Small series of cases have generally been omitted as they tend to give an erroneous impression. For example, Olow's death under nitrous oxid-oxygen, is listed among the fatalities of that agent, but his series of 14 administrations with 1 death is not included. Also when a series of cases is known to have been included in a larger series, the smaller series of cases has been omitted from the present record. Nevertheless it has been impossible to avoid some repetition of cases.

CONCLUSIONS.

From the study of the statistics of mortality under anesthetics at present available, one is able to determine approximately the relative danger attending the use of the different agents employed, but not to state exactly the degree of the danger. There is no anesthetic agent, either general or local, which is free from danger, when ignorantly or carelessly employed. Some of the deaths under anesthesia, however, are avoidable. Many could be obviated if greater attention were given to the subject.

As a remedy for the present unsatisfactory conditions, Hewitt suggests: (1) that it shall be made a penal offence for anyone not a medical or dental practitioner to administer an anesthetic; (2) that all anesthesia in hospitals or clinics shall be administered, or the administration supervised by experienced anesthetists; (3) that a course of instruction in anesthesia and analgesia shall be given in all medical and dental schools, and (4) that registration of all deaths under anesthetics shall be made compulsory. (Lancet, Sept. 19, 1908).

In no other departments of medicine, surgery and dentistry can be found the lack of scientific method which is present in the use of anesthetics. The anesthetist with years of experience does not know the amount of the anesthetic he is accustomed to administer. Often he does not know how much ether a 100 gram can should contain. As Buxton has stated: "He is forever experimenting upon his patients and the result depends upon his acumen as an experimenter." (Lancet, August, 1913).

Having no standard for guaging the work of today, there is no improvement in tomorrow's work and little benefit from years of experience. A tendency toward scientific methods in the administration of anesthetics is seen in recent work on anesthetic doses and dosage. Waller has studied "The Quantitative Estimation of Chloroform in the Tissues," (British Med. Jour., December 28, 1901); Syms has investigated "The Concentration of Chloroform Vapor in the Air from Beneath a Skinner's Mask," (Lancet, July 9, 1904); while Waller, Hewitt and Syms have reported on the "Percentage of Ether Vapor in the Open Method," (Waller: Jour. of Physiology, xxxvii; Syms: Lancet, July 9, 1904, 81; Waller: Report, British Association, Portsmouth, 1911; Hewitt and Syms: Lancet, Jan. 27, 1912).

Boothby states in his article on "Ether Percentages," that "surgical anesthesia depends on the establishment in the blood and tissues of a definite anesthetic tension, corresponding to about 15 per cent. of ether vapor in the alve-

olar air." (Journal A. M. A., Sept. 13, 1913, 830). He has also contributed a valuable paper on "The Determination of the Anesthetic Tension of Ether Vapor in Man." (Jour. Pharm. & Exper. Therap. v, No. 4, March, 1914). Connell has determined the necessary percentages of ether vapor for producing different zones of anesthesia. (Annals of Surgery, December, 1913, 877). He has also established the necessary percentages of nitrous oxid and oxygen for producing the various zones of anesthesia. (Amer. Jour. of Surg., Jan., 1915, 39).

It is to be hoped that a continuation of the scientific work begun by these observers may result in such improved anesthetic methods that it will be impossible, in future years, to chronicle such a list of fatalities under anesthetic agents, as have been here collected.

THE ANESTHETIST MUST, IN MANY INSTANCES UNDERTAKE DUTIES OF CONSIDERABLE GRAVITY, AND HE SHOULD BE THOROUGHLY EQUIPPED, NOT ONLY BY MEDICAL QUALIFICATIONS, BUT PHYSICALLY, BY POSSESSING PERFECT SENSES OF SIGHT AND HEARING, KEEN SCENT AND GENTLENESS OF TOUCH. TO HIS SHARE FALL THE PROVISION AND ACCURATE MANIPULATION OF THE BEST DRUGS AND APPARATUS FOR THE ADMINISTRATION OF THE VARIOUS ANESTHETIC VAPORS; THE DETECTION OF THE SYMPTOMS AND PHYSICAL SIGNS OF DISEASE, WHICH WILL AFFECT THE SUBSEQUENT ANESTHESIA; THE CHOICE OF THE PARTICULAR ANESTHETIC OR SEQUENCE OF ANESTHETICS MOST SUITABLE TO THE PATIENT AND OPERATION IN HAND; THE PROTECTION OF THE BODY FROM EXTERNAL HARM; THE REGULATION OF THE ATMOSPHERIC TEMPERATURE; THE RESORT TO STIMULANTS AND METHODS OF RESUSCITATION IN CASES OF FAILING VITALITY; THE SAFE TRANSFERENCE TO BED AND SUPERVISION DURING RECOVERY FROM INSENSIBILITY. THESE TASKS OFTEN INVOLVE NO SMALL TAX UPON HIS NERVOUS ENERGY AND CONSIDERABLE CALL UPON HIS TIME.

—H. Bellamy Gardner.

CARDIAC FIBRILLATION AND CHLOROFORM SYNCOPE . THE ADRENALIN SYMPTOM-COMPLEX, EXPERIMENTAL AND CLINICAL . GENERAL CONDITIONS WHICH INDUCE VENTRICULAR FIBRILLATION UNDER CHLOROFORM . SUMMARY OF OBSERVATIONS . CONDITIONS OF ANESTHESIA WHICH PRECEDE DEATH IN THE HUMAN SUBJECT . PRACTICAL CONSIDERATIONS . ANALYSIS OF STATISTICAL REPORTS . APPENDIX.

BY A. GOODMAN LEVY, M. D., R. A. M. C., LONDON, ENGLAND

THE LATEST REPORT OF the Registrar-General (1911) indicates a total estimated mortality of 243 deaths from chloroform and its mixtures in the year. This entails an incidence of two deaths every three days in England and Wales alone. The problem of the prevention of death under chloroform has evidently remained unsolved up to the present moment.

EXPERIMENTS WITH ADRENALIN UPON ANIMALS LIGHTLY ANESTHETIZED WITH CHLOROFORM.

A consideration of a number of fortuitous cases of sudden death of an anomalous type, which I had observed in animals, under the influence of chloroform anesthesia of a distinctly light degree, led me to test the action of adrenalin in chloroformed animals. The experimental results obtained with this body exceeded my expectations, though based on a theory of vascular strain, they have opened up paths of investigation which have yielded important information.

This first series of experiments with adrenalin are fully dealt with in various publications, [1] [2] [3] [4], and so it is necessary only to include a brief abstract of the subject here.

If a small dose of adrenalin chlorid, say, half a minim of the commercial 1 in 1,000 solution, be injected into a vein of a cat fully under the influence of chloroform, a well-marked rise of blood pressure will be indicated by a manometer connected with the circulation. If the dose of adrenalin be sufficiently small and the anesthesia be sufficiently deep, then the heart may be found to continue to beat perfectly regularly; more frequently, however, as the adrenalin effect devlops, the heart passes into an irregular condition of a remarkable type. The obvious features of this condition are a rapid succession of small beats, about 300 per minute, the individual beats being sometimes almost equal in size and in time incidence, sometimes more irregular and interrupted by pauses of short duration. Electrocardiographic tracings demonstrate that this irregularity is one of a singularly complex type—in fact, it frequently happens that not a single normal beat can be found in the sequence, which consists entirely of ventricular extrasystoles; that is to say, the contraction impulses arise in the ventricles themselves and not in sequence to auricular contractions. Moreover, the ventricular contractions are propagated, not from one but from many points of origin in both the right and left ventricles, constituting a condition which may be defined technically as a multiple extrasystolic ventricular tachycardia (Figures 2 and 7). After the effect of the adrenalin, which, as is well known, is only temporary, has worn off, the heart quiets down and the beat eventually becomes regular once more.

If the same injection be made into an animal only lightly anesthetized with chloroform the resulting reaction is ultimately more intense; it is, in fact, almost invariably fatal. To insure the success of such an experiment, an initial full, or nearly full anesthetization with chloroform is essential: the vapor being thereafter reduced below 1 per cent., but the corneal reflex being retained and active. It is useless to put the animal first under some other anesthetic, such as morphia or ether, and proceed with an attenuated vapor. This latter procedure has been adopted by Rothberger and Nobel with inconclusive results.

We will presume the heart, under such conditions, to be beating with a normal, regular rhythm when half a minim of solution of adrenalin chlorid is injected into a vein; the heart passes, as before, into an intensely irregular condition of the type previously described. The final result is, however, different, for before the action of the adrenalin has worn off, and whilst the blood pressure is still abnormally high, the heart, with a startling suddenness, ceases to propel blood into the arterial system, and in a graphic record the blood pressure is seen to sink to zero in the precipitate fashion shown in the tracing (Figure 1). This is an almost invariable effect.

What has happened is this: Up to the moment of the collapse of the circulation the ventricles have been

contracting in a chaotic sequence of irregular beats, but each beat is still a *co-ordinate* beat; each ventricle contracts as a whole and expels its contents, and so the blood pressure is sustained.

Now this multiple vetricular tachycardia is very liable to pass into a more serious condition, known as *ventricular fibrillation,* in which the beats are propogated at an even more rapid rate, but they are then modified beats, for the ventricles do not contract as a whole, and as a consequence they cease to exercise an active function. Authorities do not agree as to the exact nature of the beat or muscular contraction in ventricular fibrillation. Personally I have adopted the view put forth by the late Professor G. R. Mines, that a very short wave of contraction circulates rapidly *around* the ventricles, and for those who wish to inquire further an investigation of this subject in a paper by the author may prove of interest.[5] Likewise the theoretical consideration of the anomalous types of heart beat preceding fibrillation will be found in a paper by Dr. Thomas Lewis and myself,[2] in which, however, the subject of fibrillation is treated from a different standpoint. I may here express my indebtedness to Dr. Lewis, whose fund of knowledge concerning the mechanism of the heart beat has been invaluable in the course of my researches.

Now with the onset of fibrillation the electrocardiogram shows a sudden and characteristic change, which is exemplied in Figure 2. This change occurs at the exact moment the blood pressure commences the sudden fall shown at the termination of the tracing in Figure 1.

Let me here draw attention to the analogous condition of the auricles, but only to mark a distinction: fibrillation of the auricles is now a well recognized entity; it is true it causes a disordered action of the ventricles, but this is entirely of another nature, and fully consistent with the survival of the individual.

Adrenalin belongs to a group of substances which are styled by pharmacologists *sympathominettic,* of which the action is limited to structures which are innervated by fibres of the sympathetic system. This action is originated in the terminations of the sympathetic distribution, and it results in a rise of blood pressure, mainly caused by vasoconstriction in those vessels in which the constrictor fibres predominate, but also reinforced through stimulation of the augmentor nerves of the heart, which is thereby accelerated and caused to beat with increased force. This direct cardiac action is apt to be overlooked, for it is obscured by the more obvious vasoconstrictor effect, but to it and to it alone the abnormal condition which arises when adrenalin is injected into the blood of an animal under chloroform must be attributed.

This proposition is established in a further paper on: "The Genesis of Ventricular Extrasystoles under Chloroform,"[6] to which the reader is referred, as the subject is a long and complicated one. Ventricular

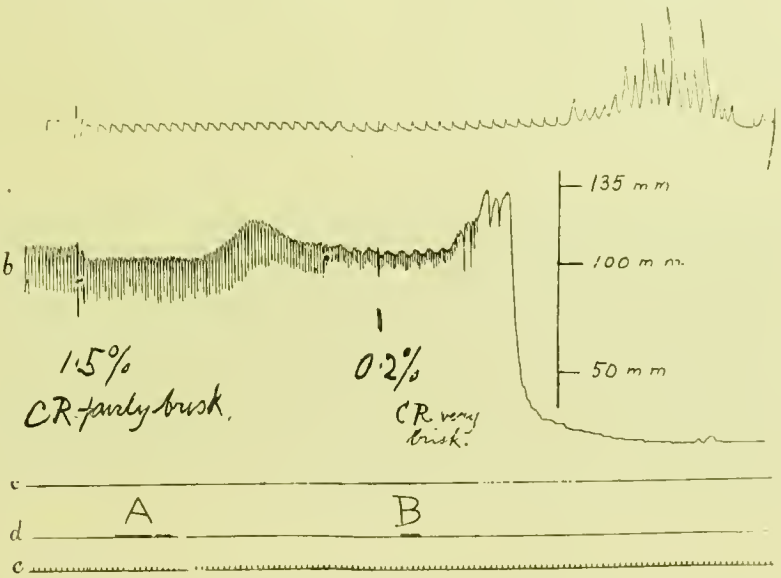

Figure 1. *a,* Respiration curve, registered from thoracic movements. *b* Blood pressure curve, registered by mercury manometer. *c,* Level of zero pressure. *d,* Signal line; each signal mark indicates an intravenous injection of ½ minim of 1 in 1,000 adrenalin solution diluted to 1 in 20,000. *e,* Time marker, indicating intervals of one second. The vertical scale indicates blood pressure levels. The tracing represents the effect of two consecutive injections of adrenalin (A and B) into the same cat under different depths of chloroform narcosis; A, under 1.5 per cent. chloroform; B, under 0.2 per cent. chloroform. The result of A is a rise of pressure only, the heart beat remaining regular. The result of B is likewise a rise of pressure, but with it the heart beat becomes small, rapid (300 per minute), and irregular, and finally ceases abruptly. This cardiac collapse occurs some eighteen seconds after the termination of the injection, and the respiratory movements, after passing through an exaggerated phase, cease also some thirty-eight seconds later.

fibrillation in cats is generally permanent and ends in death of the heart from asphyxia of its tissues, but exceptionally spontaneous recovery occurs, and this may be temporary, culminating in a second collapse, or it may terminate more favourably in a regular beat and permanent recovery. The prospect of recovery is greater when the doses of adrenalin are very small: the smallest dose I have so far found efficient in a cat has been one-fifth of a minim, and in this case recovery ensued.

The respiratory phenomena in connection with this form of heart failure are noteworthy—the bulbar centers, which are not depressed as from a full dose of chloroform, are suddenly emptied of blood, and the anemia stimulates the respiratory centre powerfully; a number of deep gasps are taken and then the respiration ceases (Figure 1). The respiratory center, however, is not yet *dead*—it has not been killed by excess of chloroform—spontaneous respirations may arouse respiration, and the late persistence of respiratory effort in the absence of heart action is a marked feature in many of these deaths.

In animals not under the influence of any anesthetic adrenalin does not produce irregularities of the nature

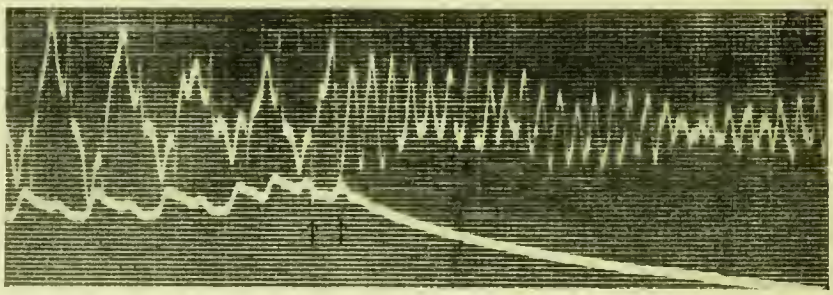

Figure 2. Upper curve, electrocardiographic. Lower Hürtle Manometer. In the first part of the tracing the E. K. shows a succession of extrasystoles arising alternatively from the right and left ventricles, (rate about 300 per minute). The first arrow marks the last extrasystole; the second arrow marks the corresponding pulse—beat in the Hürtle curve. Thereafter the ventricles are fibrillating; the blood-pressure immediately begins to fall and the characteristic E. K. of ventricular fibrillation is seen.

I have just described, and under ether I have employed very much large doses of adrenalin than those which react under chloroform, up to 5 minims of the 1 in 1,000 solution, in fact, with the result that lesser degrees of irregularities were exceptionally observed, and never fibrillation.

The adrenalin reaction has not been thoroughly worked out in animals under the influence of mixtures containing chloroform, such as the A. C. E. mixture; but it is certain that in any condition in which chloroform is exhibited a similar danger of a reaction to adrenalin exists. Recent, hitherto unpublished, experiments have shown that a sufficient initial dose of chloroform, whether alone or in mixture, must be given to render the heart susceptible to the adrenalin reaction, which occurs when the dose of chloroform is subsequently reduced. It is possible, therefore, that if extremely small quantities of A. C. E. mixture are administered, the subject may become very lightly anesthetized without ever becoming sufficiently under the chloroform component to become sensitive to adrenalin. It would be unsafe, however, in my opinion, to apply this consideration in practical anesthetics.

THE ADRENALIN REACTION IN THE CHLOROFORMED HUMAN SUBJECT.

A communication in regard to this matter was read some time ago before the British Medical Association,[3] and it was therein shown that fatalities have occurred from the ill-advised use of adrenalin for surgical purposes and for the treatment of shock in patients under chloroform. It was shown, moreover, that the anesthesia was a light one at the time of injection and that the mode of death was similar to that which occurs in cats under similar conditions. The only difference noted was a pronounced tendency to recovery in the human subject.

Since the publication of this paper a considerable number of similar accidents have been reported, and other unreported cases have come to my knowledge; many of them occurring as the result of the injection of adrenalin into the mucous membrane of the nose, in the course of an operation for deflected septum, and a few of the fatalities have also occurred as the result of intramuscular injections. In all these cases the anesthesia was of a light degree. I believe that the danger of injecting adrenalin under chloroform anesthesia is now fully recognized and that the procedure has been abandoned, both in England and elsewhere.

A single report of such a fatality will serve to call attention to the dangers involved in the procedure:

ILLUSTRATIVE CASE: The patient was a male aged 26, a well-developed and healthy man. Operation for deflected nasal septum. Anesthesia was induced by chloroform given upon a Skinner's mask, and it was decided to inject some adrenalin into the nose, subcutaneously. At the time of the injection anesthesia was light (a brisk corneal reflex being obtainable), the pulse was very strong and the patient's color good. No more chloroform was given. About one minute after the injection the pulse suddenly became very rapid and then imperceptible; at the same time the patient's color became leaden grey and the pupils widely dilated. About three deep gasps were taken after the pulse had failed and then respiration ceased. (British Medical Journal, 1913, Vol. I, p. 879).

It is maintained by some anesthetists, from clinical experience, that irregularities of the pulse are less liable to be noted on the injection of adrenalin under very light anesthesia with chloroform and ether mixtures, the patient being barely analgesic. This may be the case in many instances, as previously noted, but I feel sure that it is not possible to adjust the administration to such a nicety as to render the proceeding safe.

GENERAL CONDITIONS WHICH INDUCE VENTRICULAR FIBRILLATION UNDER CHLOROFORM.

I have dealt with the chloroform-adrenalin reaction at length, as a proper understanding of it is essential in order to grasp what is to follow.

The form of cardiac irregularity induced by adrenalin may also be induced by a number of other diverse agencies acting in animals under light chloroform anesthesia. Adrenalin may be regarded simply as a very potent form of a *cardiac stimulant*, employing the term *stimulant* in its widest sense, and I find, as a result of a prolonged investigation,[4] that these and other agencies, pharmacological and physiological, (those that have a similar cardiac effect in the presence of chloroform only, and not when acting *per se*), likewise act in some way as a *cardiac stimulant*, and therein lies the germ of my theory in respect of sudden death under chloroform.

Broadly speaking, chloroform does not in itself induce ventricular irregularities, but it renders the heart *irritable* and liable to exhibit such subnormal contractions under influence of certain exciting causes, and such exciting causes consist of *diverse forms of cardiac* stimulation.

The effect of cardiac stimulation naturally varies in its intensity or may be modified by antagonizing agents, (such, for instance, as exaggerated vagal action), but provided the heart be only lightly affected by chloroform, ventricular extrasystoles will almost certainly appear as a result, and if they appear in a rapid sequence then they may terminate as ventricular fibrillation. If the heart be more fully affected by chloroform and the stimulation be intense these irregularities may still appear, but they never terminate in ventricular fibrillation; generally even the irregularities are suppressed. This controlling and protecting influence of full anesthetic concentrations of chloroform upon the heart is a *fundamental point in the* consideration of the cause of death under chloroform; it is, I believe, connected with the depressing influence which chloroform exerts upon the heart, and influence, which, as is now well established, is manifested in a progressive fashion as the strength of the vapor is increased.

The more intense forms of ventricular irregularities have already been described and illustrated. Less intense forms of ventricular irregularities occur as a result of cardiac stimulation under intermediate degrees of chloroform anesthesia, or from very slight stimuli under light anesthesia. The less intense forms of irregularities form a sequence, from isolated ventricular extrasystoles through groups of periodically recurring extrasystoles (so-called *trigeminal* and *bigeminal* beat), and through a complicated mixture of normal beats and extrasystoles, up to the dangerous condition of a multiple tachycardia.

These simpler forms of irregularity are illustrated in Figures 3 and 4; the multiple

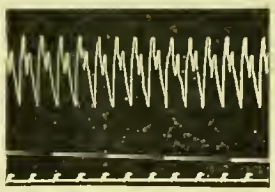

Figure 3. Rythmical extrasystoles occurring under light chloroform anesthesia. The tall peaks are normal heart-beats; the alternate small peaks represent extrasystoles, and they are followed by a pause indicated in the tracing by a drop in the blood-pressure. The alternating normal and extrasystolic contractions constitute the "bigeminal pulse." Hürtle manometer. Time marked in seconds. (Natural size.)

tachycardia is typically exemplified in Figure 5, and in the latter part of Figure 6. The difference in the tracings, according as a membrane manometer (Hürtle) or a mercurial

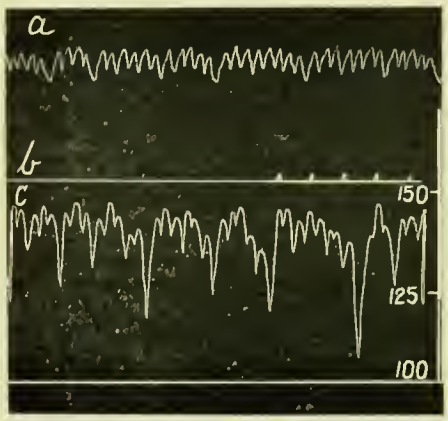

Figure 4. Hürtle and Ludwig curves recorded simultaneously from separate carotid arteries. *R.* Respiratory curve. *a.* Hürtle curve. *b.* Hürtle abscissa and time signal marking seconds *c.* Ludwig curve. The Ludwig abscissa is not shown. These curves illustrate a rapid type of irregular tachycardia under chloroform. The Hürtle manometer accentuates the individual pulse beats, often, as in this case, with little appearance of irregularity. The mercury manometer accentuates the irregular nature of the curve, but tend to obliterate the individual beats. The fluctuations in pressure bear no relation to the respiratory rhythm. Rate of beat—270 to 300 per minute.

manometer (Ludwig) is employed should be noted in these tracing. The Hürtle manometer accentuates the individual pulse beats and the mercurial manometer, while accentuating the irregular nature of the curve, tends to obliterate the original beats. The mercurial manometer likewise affords a true measurement of the blood pressure, which cannot be gauged by simple inspection or the use of the membrane manometer. Electrocardiographic tracings illustrating various types of irregularities are shown in Figure 7.

I will now briefly describe some of the more important forms of cardiac stimulation which are liable to produce a fatal reaction in the lightly chloroformed animal:

(1) STIMULATION BY EXCITATION OF THE MYONEURAL JUNCTIONS OF THE SYMPATHETIC CARDIAC NERVES (*accelerator nerves*), AS BY ADRENALIN. This reaction has already been dealt with, it is a very powerful form of stimulation, and almost invariably leads to ventricular fibrillation under properly regulated anesthesia.

(2) STIMULATION OF THE ACCELERATOR NERVE-FIBRES BY ELECTRICAL EXCITATION, results in ventricular fibrillation in about two-thirds of the experiments performed, the sequence of events in positive cases being almost precisely similar to that observed in the adrenalin experiment, Figure 6. Not only are the manometer curves identical, but the electrocardiographic tracings in the two cases are likewise identical, and there can be no possible doubt that an identical process is involved in each of these reactions. Similarly death occurs during light anesthesia only and not during deep anesthesia.

(3) STIMULATION BY ACCELERATOR IMPULSES ORIGINATING IN THE CENTRAL NERVOUS SYSTEM, such as may accompany the sub-conscious emotional state of a struggling animal. This is a very usual precursor of ventricular irregularities, and occasionally of ventricular fibrillation. Struggling is a common precursor of death in an animal which is being put under chloroform, and this struggling is of course *prima facie* evidence of imperfect anesthetization.

There is, however, a difficulty, obvious to all who are familiar with physiological technique, in obtaining graphic records of animals in the early stages of anesthesia, but by special methods, I have succeeded in obtaining one

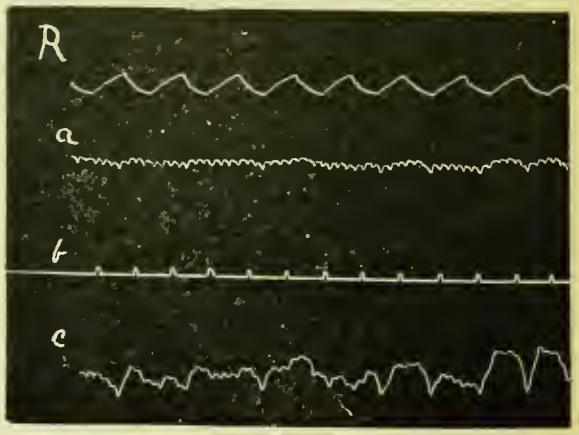

Figure 5. Contrasted Hürtle and Ludwig curves, recording consecutive periods of an irregular tachycardia with beat rate of 180 per minute. *a.* Hürtle curve. *b.* Hürtle abscissa and time signal marking seconds. *c.* Ludwig curve. *d.* 100 mm. mercury pressure level.

such record exemplifying sudden death from ventricular fibrillation in the struggling animal, Figure 8.

As regards the mode of action of struggling, I think it can hardly be doubted that the onset of irregularities is the outcome of a state of general nervous excitement, which affects the sympathetic as well as the somatic nerve paths. The subjective evidence of cardiac acceleration in emotional states is a commonplace observance; apart from this it has been shown by Cannon and de la Paz,[7] and later confirmed by

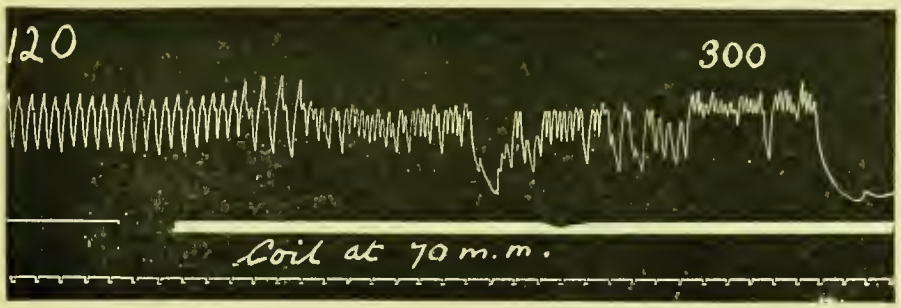

Figure 6. Excitation of the cardiac accelerator nerves with a faradic current, in a cat under 0.5 per cent. chloroform. The heart-beat becomes highly irregular and interrupted by short pauses, and finally fails abruptly and permanently in ventricular fibrillation. The figures above the curve indicate rates of heart-beat. The signal mark indicates the duration of the faradic excitation. Hürtle manometer. Time marked in seconds. (Natural size.)

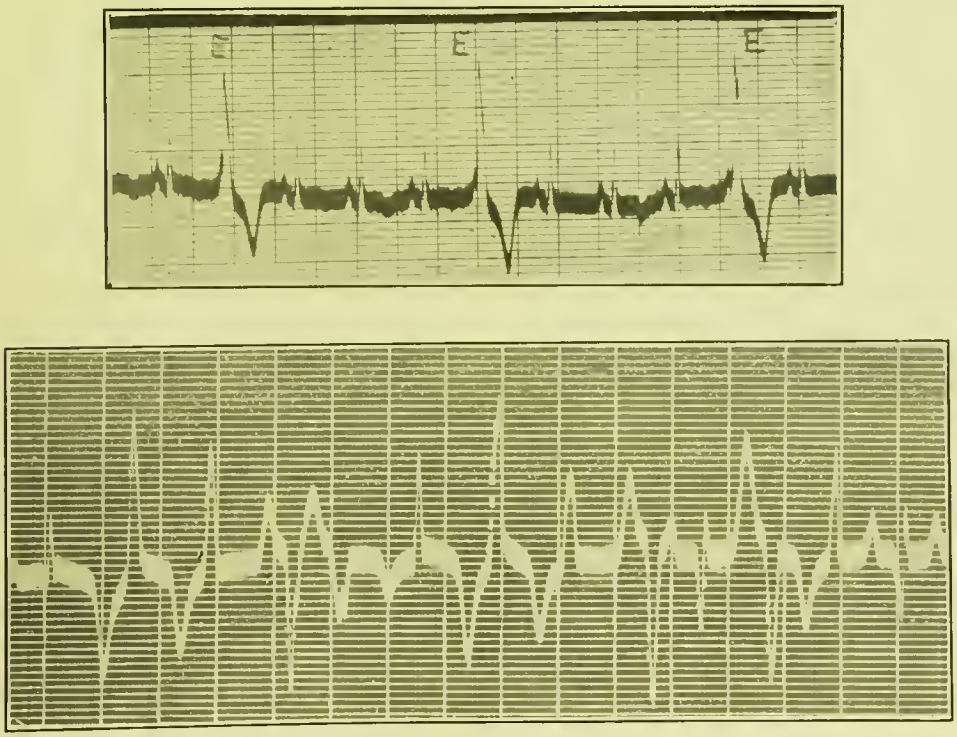

Figure 7. Electrocardiograms of the heart beat under chloroform. Cat. The vertical lines indicate intervals of 1-5 second.

(A) Every fourth beat is a ventricular extrasystole, the intermediate beats are normal.

(B) A "multiple ventricular tachycardia." Every beat is a ventricular extrasystole, and each is of a different type. Rate of tachycardia about 240 per minute.

Elliott,[8] that emotional states, such as fright or anger, are accompanied by an increased secretion of adrenalin. In this way in all probability a double effect, accelerator and suprarenal, is brought to bear on the heart.

Ventricular fibrillation may also be produced under chloroform in the course of convulsions produced through the action of strychnin or by *pithing* the spinal cord, and, in fact, I conclude that under conditions of light chloroform anesthesia, any convulsive nervous output, such as that which may be said to accompany struggling, may result in cardiac syncope from ventricular fibrillation.

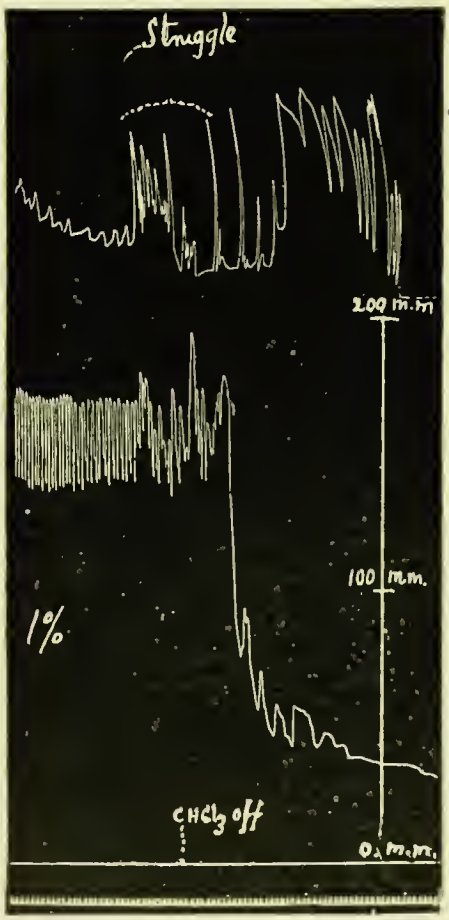

Figure 8. Ventricular fibrillation caused by struggling during the induction period. Upper curve respiratory. This shows a declination in its first portion caused by a leak in the recording apparatus. Lower curve blood-pressure, registered by a mercury manometer. Time marked in seconds. Anesthesia induced by 1.5 per cent. chloroform, then 2 per cent., then reversion to 1 per cent. when the animal began to struggle. The heart became very irregular, the chloroform was entirely removed, and the ventricles fibrillated a few seconds later. The fluctuations in the blood-pressure during struggling are mainly mechanical, and the small irregular beats are almost obscured in the reproduction; ventricular fibrillation is indicated by the abrupt fall of blood-pressure. The final fluctuations at the foot of the pressure curve are caused by the powerful asphyxial respiratory gasps, which are delineated in the respiration curve. The heart was inspected immediately on the cessation of respiration, and the *ventricles were found in a state of coarse fibrillation.*

The following straight-forward experiment, in which no experimental operative procedures were adopted, serves to illustrate syncope of this nature:

ILLUSTRATIVE EXPERIMENT: Cat 6. Cut male. 2,455 grms. 2.59 p.m. 1% *ad plenum*, on. (The term *ad plenum* is employed to denote the administration of vapor in excess of the respiratory requirements: the vapor being drawn through a regulating inhaler and delivered, mixed in measured percentages with air, through a metal funnel supported over the head of the animal. The respirations are in this way entirely natural and unhampered.

The type of inhaler employed[9] was one designed to work by the force of human respiration, but which can be readily adapted for laboratory work by means of a suction and delivery pump, the only additional fitting required is an elastic bag to render continuous the intermittent stream from the pump).

3.3 p.m.	Spasmodic movement and phonation.
3.3½	Struggling. Chloroform off; heart becomes irregular.
3.4½	1% on.
3.6½	Struggles strongly. Heart suddenly ceased beating; respiratory spasm and loud phonation ensuing.

The literature of death under chloroform in man teems with references to struggling as a precursor of death, so that it is unnecessary to give particular instances. In these cases the anesthesia is manifestly light; the contention that deep gasps are made during struggling and the heart is thereby stopped by the excessive intake of vapor is a pure figment of the imagination and totally devoid of experimental confirmation; an absolutely sudden stoppage of the heart by overdosage has never been demonstrated and as a matter of fact the respiration is *restrained* during struggling under partial anesthesia; the deep gasps come indeed, as has already been indicated, *after the actual cessation of the heart beat.* Further in many of these clinical cases the anesthetic had been entirely removed when death occurred.

There can be only one explanation of death in such cases, and that is through ventricular fibrillation.

(4) STIMULATION BY ACCELERATOR IMPULSES ORIGINATING AS A REFLEX FROM THE

EXCITATION OF SENSORY NERVES. Experimentally, irregularities are very readily induced by comparatively mild forms of sensory excitation such as cutting the skin, or more certainly by cutting, or applying a faradic current to nerve trunks containing sensory fibres. As *a relatively rare event,* ventricular fibrillation is a sequence to irregularities induced in this reflex way.

In this instance the depth of anesthesia is doubly important, for the reason that full anesthesia effectively blocks sensory reflexes, in addition to depressing the heart. The experimental work associated with sensory cardiac reflexes is fully dealt with elsewhere.[4] I may merely point out here that the tracings illustrating death from sensory reflexes are essentially similar to that shown as a result of direct sympathetic stimulation, Figure 6; a single tracing, Figure 9, is given for comparison.

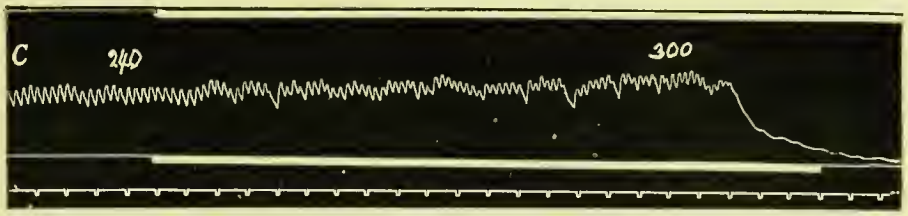

Figure 9. Sciatic stimulation in a cat under 5% chloroform. Heart somewhat irregular before stimulation; the irregularities become more pronounced during stimulation and terminate in syncope from ventricular fibrillation. Hürtle curve. Time in seconds. The signal marks period of stimulation. The numbers indicate the rates of heart beat.

Likewise I may refer to the interesting and demonstrable fact that a reflex secretion of adrenalin from the suprarenal bodies is an accessory factor in causing death.

It cannot be doubted that deaths occur in this fashion in the human subject. Death has been frequently described as occurring *on the first touch of the surgeon's knife* and a considerable proportion of fatalities occur in the course of trivial but painful operations in which the minimum amount of chloroform has been administered on account of the shortness of the operation.

Unfortunately there are few absolutely precise records of the events accompanying death under chloroform in man; naturally this is not a fitting moment for making scientific notes of pulse and respiration, and accounts written subsequently are generally confused, especially in regard to the time relation of events. Here and there, however, clear descriptions may be found; to illustrate my point I will confine myself to a single striking case described by Dr. Alex. Wilson, Senior Anesthetist to the Manchester Royal Infirmary:

ILLUSTRATIVE CASE: "The patient, a girl of fifteen years of age, was operated on for *genu valgum* by Macewen's method. Chloroform was given on lint; she took it well, the operation was performed, and the splint in process of being put on. At this stage, under the impression that all painful operative procedures were completed, the anesthetic was discontinued. The patient was then breathing quietly; she had a good pulse and normal color; the pupils were slightly contracted, and the corneal reflex was present —in fact, she was coming out of the anesthetic, but was *sufficiently insensible to bear ordinary manipulations or even incisions without feeling pain,* and was as well as anyone could wish her to be. At this instant the surgeon suddenly forcibly flexed the left knee, which was stiff owing to osteotomy having been performed on that side a few weeks previously. The adhesions gave way easily with a crunching sound, and the patient uttered a scarcely articulate cry, immediately became deadly pale, and began to breathe deeply. She passed at once into the following condition: the head was turned to one side, the face was deadly pale, the eyes were slightly open, the pupils were widely dilated, and she was taking deep inspirations, the air passing freely into the chest; the muscles of the alae nasi were also acting, and the pulse was imperceptible at the wrist. The symptoms conveyed the impression that she had fainted. To drop the head, elevate the limbs, and apply hot sponges, was the work of a moment. She continued to make strong respiratory efforts, and air was freely entering the lungs, but there was still no sign of the radical pulse. It appeared at first that the patient would probably recover—it seemed impossible that she could die with such active respiration; but the breathing, without shading off in the least, suddenly ceased, and every effort to restore life failed." (Lancet, 1894, Vol. II, p. 1148).

Can a death of this description be ascribed to any cause other than ventricular fibrillation?

It is absolutely certain that death in this

particular instance was not conditioned by *overdosage*. There is a prevalent idea that sudden death may result from the reflex inhibition of the heart through the vagi. No vestige of direct experimental evidence can be adduced in support of such a view, despite the innumerable attempts to produce a fatal vagal

tained a condition even approaching permanent inhibition.

(5) STIMULATION BY RELEASE FROM DEPRESSING OR RESTRAINING INFLUENCES, or as I term it, *passive stimulation*. This is well exemplified in the result of section of the vagi; the heart, when lightly influenced by chloro-

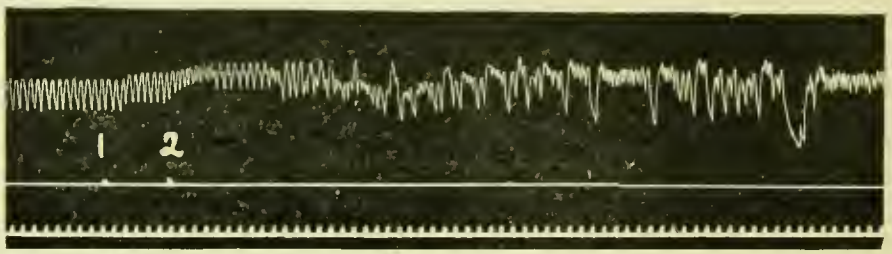

Figure 10. Section of the vagi in a cat lightly anesthetised by 0.5% chloroform. Previous to vagotomy the heart was beating regularly at a rate of 90 per minute. On cutting the vago-sympathetic nerve trunks in the neck (signal marks 1 and 2) the heart accelerates and the blood-pressure is forced up. The beat then by gradual stages becomes more and more irregular with momentary periods of ventricular fibrillation. Hürtle manometer. Natural respiration. Time marked in seconds. The signal line has been adjusted to the Hürtle abscissa.

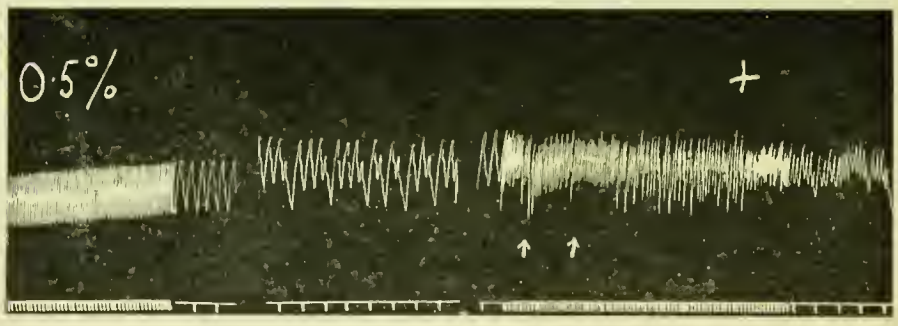

Figure 11. The effect of abruptly reducing the strength of chloroform vapor from 2 per cent. to 0.5 per cent. Portions of the tracing have been cut out in order to reduce its length; the first interval represents a period of 115 seconds, the second interval a period of 35 seconds. The time-marked indicates second; the spacing of the time marks differs accordingly as the paper was moving at a quick or slow rate. At the beginning of the tracing the vapor was reduced, the heart-beat then being regular, blood-pressure=84 mm. Hg. In the middle section the blood-pressure has risen to 114 mm.; extrasystoles now appear at irregular intervals. In the third section no chloroform was inhaled for the short space indicated between the arrows. At the mark + the irregularities assume a more intense form, that of a multiple tachycardia, and a little later the ventricles pass into fibrillation and the blood-pressure falls to zero in consequence. Hürtle manometer. (Natural size.)

reaction in the chloroformed animal. Permanent inhibition of the mammalian heart by reflex vagal action remains unknown to experimental physiology.

A series of experiments involving reflex cardiac inhibition under chloroform are included in a paper by the author.[16] I never ob-

form, becomes highly irregular, and not infrequently the ventricles ultimately fibrillate. Figure 10. *Entirely analogous to this* is the result of reducing the strength of the chloroform, or removing it altogether; the heart responds by gathering force and frequency of contraction, and in consequence it very usually

becomes irregular; if it becomes highly irregular sudden syncope from ventricular fibrillation may be observed, sometimes attained with startling rapidity, *but fortunately this climax is an exceptional event.* Figure 11.

This effect may be observed in the earliest stages of the administration, but it has been frequently observed also in cats after removing the chloroform on the completion of an operation, particularly when excitement occurs on recovery, occasionally when the animal is perfectly quiescent. The animal is particularly liable to die in this way after a short administration, or after a more prolonged operation under restricted doses of chloroform; it may then occur within a minute or two or may be deferred so long as fifteen minutes.

Two examples out of numerous experiments of this kind in cats are here quoted in illustration.

ILLUSTRATIVE CASE 1: August the 2nd, 1912. *Ad plenum* method.

2% chloroform *ad plenum*, for three minutes, breathing quite quietly, not deeply under at any time, heart beating quietly, not fast, corneal reflex present, not very active. At the end of three minutes chloroform removed as an intentional test, respiration increased in force almost at once, no struggling, phonated, and breathed deeply. No heart beat felt when spasm of chest had passed.

P. M. Ventricles fibrillating. Right auricle purple, left auricle bright red.

ILLUSTRATIVE CASE II: August the 2nd, 1911. Cat. Induction with 2% chloroform, *ad plenum* method. When under, the chloroform was reduced to 1-5% whilst the neck was being shaved. The chloroform was then taken off and a bandage rolled round the neck, and then the animal was laid on its side on a bench to recover. A few minutes later the cat commenced the *running* movements which are so frequently a sign of returning consciousness. These movements ceased suddenly within a few seconds of their appearance, powerful expiratory efforts made their appearance accompanied by loud phonation, and on cessation of respiration no sign of heart beat could be found.

P. M. Chest opened rapidly. *Ventricles fibrillating.* auricles beating, right auricle purple, left auricle bright red.

In the human subject intermission, or entire removal, of the chloroform may frequently be traced in the procedure which prefaces the death of a patient; on this subject I shall have more to say later. Death after completion of a short operation, when the administration has entirely ceased, is a not uncommon event, more especially in adults; in young children it would appear that a considerable degree of immunity to ventricular fibrillation exists.

In those cases in which the patient dies during recovery from anesthesia on completion of an operation, the anesthetist's attention is usually relaxed and precise details are in consequence lacking. The following is a typical report of this kind:

ILLUSTRATIVE CASE: "A boy aged fifteen years, had been anesthetised with chloroform for the removal of post-nasal adenoids. The operation had been completed and the anesthetic withdrawn, when the patient was noticed to be breathing deeply. The operator observed some peculiarity about the color of the face, but was reassured *by the presence of free respiration.* The respirations, however, suddenly ceased, and all efforts to resuscitate the patient failed." (Lancet, September 11, 1897).

(6) STIMULATION BY RE-APPLICATION OF THE VAPOR AFTER AN INTERMISSION, OR IN THE COURSE OF A VERY LIGHT ADMINISTRATION. When first noted, I was unable to decide whether death was a *post hoc* or *propter hoc* effect of reapplication, but the great infrequency with which the two events have been associated, leaves no room for doubt that the one is the exciting cause of the other.

Death may be brought about by the reapplication of chloroform vapor of ordinary anesthetic strength, at or under 2 per cent. strength, as the following experiment shows:

ILLUSTRATIVE CASE: Cat under 2% chloroform from beginning. Rapid heart beat. Quiet for first two minutes of induction, then commenced to sneeze, inhaler removed for about thirty seconds, corneal reflex active. Inhaler re-applied when sneezing had ceased. Amplitude of thoracic respirations almost immediately increased, inflated chest with expiratory groans, heart could not be palpated on account of the tense chest walls. When respiration ceased, as it did quickly, heart beat could not be felt. At the moment of reapplication the inhaler was yielding exactly 1.9% vapor.

P. M. Chest opened at once. Ventricles fibrillating.

Death from this cause appears to be more readily conditioned by employing vapor of higher concentration. I have on several occasions been enabled to obtain tracings showing ventricular fibrillation as a result of reapplying a concentrated vapor to an animal not under any anesthetic at the moment. Figure 12 shows this reaction very well. In this case the reaction was almost instantaneous, as it generally is, but it may be delayed as much as 30 seconds from the moment of reapplication. It is conclusively shown in this tracing that the cardiac syncope was not the result of an *over-*

dose in the ordinary sense of the word, although the vapor was certainly strong, for there was not sufficient time, before syncope occurred, for the vapor to produce any depressing effect, as is evidenced by the fact that the blood-pressure at its final elevation was 152 mm. The cat was, in fact, still lightly anesthetized when it died.

The fact that the reapplication effect is more readily observed when the vapor is strong constitutes, so far as I have observed, the only particular instance in which a strong vapor more readily conduces to ventricular fibrillation than a weak one, and this greater facility of causing syncope with a stronger vapor in this single set of circumstances has, I believe, *been mainly responsible for the support which has been accorded to the idea that all deaths under chloroform are the result of overdosage.*

When a strong irritating vapor is given suddenly to a lightly anesthetized cat it may, and often does, cause the animal to struggle, and this struggling alone may then of course account for fibrillation. When struggling does not occur, a slight general muscular twitch is frequently observed at the moment of reapplication; the animal appears to become slightly tense, as was the case in the experiment from which Figure 12 was taken, and this fact points to the probability that the onset of fibrillation is conditioned largely by a reflex sensory stimulation. (A reflex vaso-constrictor effect may be readily demonstrated in a cat under atropin on reapplication of chloroform).

Apart from the above considerations it appears probable that the first effect of chloroform upon the heart is a stimulating one, and there is in fact direct evidence of this in some experiments by Sherrington and Sowton.[10] The effect is perfectly evident and is remarked upon by the authors. In this respect chloroform shares with most other anesthetics the property of being a stimulant in the initial stages of its action.

It is, therefore, highly probable that the effect of resubjecting the heart to chloroform, after having allowed the former effects of the anesthetic to partially wear off, is a further stimulation of the ventricles through both reflex and direct means, and in this way constitutes a further exciting cause of ventricular fibrillation.

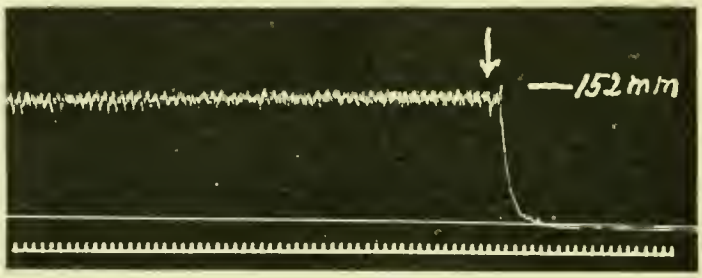

Figure 12. Ventricular fibrillation resulting from the sudden administration of a concentrated vapor to a cat *which had not been inhaling any chloroform for two minutes*, the heart exhibiting a rapid irregular tachycardia. The animal was perfectly quiescent but the application caused a slight general reflex spasm, and was almost immediately followed by V.F. The arrow marks the moment of reapplication. Hürtle manometer. Time in seconds.

SUMMARY OF FOREGOING OBSERVATIONS.

These foregoing observations may be summarized thus: Deaths from ventricular fibrillation under chloroform may be observed under any of the following and allied conditions.

(A) During the induction and early stages of the administration of chloroform and exceptionally later in the administration; (1) during struggling and excitement; (2) on removal of the chloroform; (3) on abrupt readministration of chloroform after removal, or its sudden increase during a period of very light anesthesia, and (4) by any combination of these occurrences.

(B) During operation. By strong sensory stimuli under light anesthesia.

(C) After operation. On removal of the chloroform, especially after a short operation.

Clinical illustrations of conditions (B) and (C) have already been given in the text. Clinical illustrations of conditions (A) are found in the majority of cases of death under chloroform.

The exact procedure adopted during induction is rarely recorded in reports of chloroform syncope. The method is generally an intermittent one, and is frequently characterized by a *want* of method. The patient may be inhaling chloroform one minute and inhaling none the next, so that the administrator may be unaware of the extent of the intake of vapor, much less be able to report it.

I give here a single instance of a completely reported case taken from Snow's book: *On Anesthetics;* it serves as an excellent clinical counterpart to some of the cases of death during induction in cats related in this paper, all the three causal factors of syncope, viz., excitement and struggling, intermission and reapplication being particularly well defined. There can be no question but that this man died from ventricular fibrillation.

ILLUSTRATIVE CASE: The patient, a man, thirty years of age, was affected with hydrocele. The chloroform was poured on a little cotton, which was placed at the small end of a cone, into which the folded towel made use of was rolled. About a drachm and a half was first poured on the cotton, and the patient was told to inhale in long and deep inspirations. This quantity being nearly evaporated in two or three minutes, a drachm more was added. After a few inspirations rigidity and struggling came on; these subsided, but in a little time returned more strongly than before, and the towel was removed from the face until the struggling ceased. The patient, however, not being sufficiently insensible to undergo the operation with the necessary quietness, the towel was reapplied, when, after a few inspirations, the pulse suddenly ceased. The face and the whole surface of the body turned pale, the eyes rolled upwards and inwards and the breathing became very slow, but full and deep, the intervals between the inspirations becoming longer, until the respiration ceased altogether. The patient died before the operation was begun, and within five minutes from the commencement of inhalation. During the application of various means of resuscitation, including the dropping of cold water *guttatim* on the epigastrium, the breathing returned and continued for the space of three or four minutes; but the pulse and sounds of the heart did not return."

A consideration of the foregoing observations led me to adopt a method of administering chloroform to cats which insured a *perfectly continuous administration combined with full dosage.*

I induced anesthesia more rapidly by giving the animal a fairly full percentage of vapor, 2%, or thereabouts, to inhale from the commencement. The administration was made a perfectly *continuous* one, never on any account intermitted, and the strength of the vapor never reduced; if the animal struggled it was firmly restrained, and the struggles were not allowed to interrupt the administration.

As soon as the cat began to become relaxed the vapor was generally increased slightly, up to 2.5% or occasionally 3% to bring it fully under the chloroform. I have now had an experience of some 400 cases of chloroform anesthesia induced by this method, with a single instance of death and this death followed the accidental interruption of the administration through a rubber supply tube becoming temporarily obstructed. This experience is in striking contrast to that appertaining to the usual intermitted method of administration in common use, and which has led to the disuse of chloroform as an anesthetic in many physiological laboratories.

The employment of measured doses of chloroform is not an essential factor in the administration, although it is a convenience. I am informed that equally successful results are obtained by placing a cat in a bell jar or box with an unmeasured quantity of chloroform on cotton wool to keep it company. When the cat falls down perfectly relaxed and immobile it is considered fully anesthetised. This method certainly insures the essential factor of continuity; and if enough vapor of sufficient concentration is provided (dependent on the size of the receptacle and the amount of chloroform) I should judge the method essentially safe.

A simple modification of method thus fully solves the problem of dealing with the very serious mortality in cats which occurs when anesthesia is induced with chloroform by unrestricted and haphazard methods. It remains to consider the question of the cause of death under chloroform in man and how to prevent it.

THE CONDITIONS OF ANESTHESIA WHICH PRECEDE DEATH IN THE HUMAN SUBJECT.

I have now given a fairly complete account of death from ventricular fibrillation. The

question now arises, what proportion of deaths occurring in the human subject may be attributed to ventricular fibrillation?

An essential part of my theory is the fact that deaths by ventricular fibrillation occur only in the lightly anesthetized subject, and it hence stands in clear contrast with the accepted explanation of death under chloroform by overdosage. The symptoms of overdosage are familiar: The respirations and the pulse become progressively more feeble; the respiratory functions are generally the first to fail, and according to some authorities invariably the first; let it suffice for the moment to admit that the overdosed subject, with circulation and respiration strongly depressed, may be in a critical condition.

The symptoms of death by ventricular fibrillation are different. The heart stops as an unexpected event, and with startling suddenness. The respirations are not depressed at the moment, and therefore are exaggerated as a result of cerebral anemia; later they cease entirely. There is a persistent tendency towards recovery of the respiration, often continuing long after the heart has ceased to beat, and should the latter recover the breathing is immediately resumed. A secondary cardiac syncope, with its attendant gasping respiration, may supervene on a temporary recovery, and thus there arises occasionally some confusion in the clinical interpretations of the true order of events. Sudden anemia likewise excites the spinal motor nerve centers of the skeletal muscles; some evidence of muscular convulsions is therefore generally observed, and in very lightly anesthetized subjects these may be a pronounced feature of death by ventricular fibrillation; the *epilepti-form fit,* which has been in some cases described as preceding death, is probably an asphyxial convulsion succeeding syncope.

There is one symptom which may be observed in man and which cannot be observed in the cat, and that is sudden and intense pallor; this is associated with another striking symptom—sudden and extreme dilatation of the pupils. The performance of artificial respiration may restore a pink tinge of color to the face by setting up a slight mechanical circulation, but this is of course deceptive as regards the function of the heart, which is still entirely in abeyance.

These two rival theories, underdose *v.* overdose, may be fairly submitted to the arbitration of clinical experience, and this test I shall now proceed to apply in the form of a collection of reports of fatalities under chloroform. In considering these reports it must be borne in mind that a patient cannot be made to pass, even by extreme measures, from a state of light anesthesia into one of profound narcosis or overdose in a few seconds; in effect, a patient cannot be struggling at one moment and profoundly anesthetized the next.

The following point must also be considered: A certain quantity of chloroform must be employed, and a certain dose proportionate to the body-mass must be introduced into the body, in order to produce symptoms of overdosage. The importance of regulating the strength of vapor has been so strongly insisted upon that one is likely to lose sight of the above fact. We may take it,[11] that not less than 2 dr. of chloroform in a closed inhaler, or 4 dr. on an open mask, administered in a full concentration, are essential to produce respiratory failure in an average adult. In many of the following cases the amount of chloroform employed was evidently carefully measured, and details such as these afford assistance in forming a judgment regarding the degree of narcosis involved. All cases in which not more than 1 dr. was used by open method or inhaler have therefore been excluded from the category of death from overdosage.

The collection of cases which I shall submit to analysis is that found in the Report of the Anesthetics Committee of the Royal Medical and Chirurgical Society, and issued in 1864.[12] In this report 109 cases of fatalities are briefly summarized and commented upon. In many cases, but not in all, the original references are available, and from these I have in several instances obtained important supplementary information. I have found it necessary to exclude 11 of these cases as they are absolutely lacking in detail; the numerical references to these excluded cases are given in the appended table, as are likewise those of all the remaining cases, under separate headings. Thus there remain 98 cases to be dealt with, and the percentages mentioned are

expressions of a proportion to this total of 98. *No less than 47 (or 48 per cent.) are described by the Committee as lightly anesthetized at the time of death*, the terms employed are "incomplete anesthesia," "commencing to inhale," "stage of excitement," "not fully under," and in one case "under the influence of chloroform." I give the reference number of these cases, but they require no further comment, they speak for themselves. The remaining cases are for the most part described as "fully under," or else no specific comment is made. In 14 of these cases I find definite evidence that the patients were only lightly anesthetized at the moment of death, and I have inserted in the table very brief abstracts of these reports in support of my contention. Thus *in 62 per cent. of the cases it is demonstrated that the patients died under light anesthesia.* In 24 other cases, although no definite symptoms of light anesthesia are described, it is possible to exclude overdose as a cause of death. These cases are likewise briefly abstracted; it will be noted that in the majority of instances the chloroform had been entirely removed when death occurred, and there can be no stronger reason than this for excluding the possibility of death from overdosage. It thus appears that in *87 per cent of the cases death was not caused by an overdose.* In six other cases the evidence is not so definite, but I consider that death by overdose is improbable; I cannot support this contention in a brief abstract, for the original reports must be carefully considered. Thus *in 92 per cent. death by overdose could either be excluded or was improbable.* I do not venture to express an opinion upon the details available of the remaining seven cases; there is a strong suspicion of underdosage in several, in some of the others there appears to be a possibility of death from overdosage, *but in not a single instance out of the whole 98 cases is there any definite evidence that the patient died from overdosage.*

One cannot, I am sure, fail to be impressed with the fact that some 87 per cent. of deaths are not caused by overdosage, and therefore can be accounted for by no other theory than that of fibrillation of the ventricles; I believe the actual facts are even more impressive than this, and that of the remaining 13 per cent. a large majority must be included in the same category; a few of them may be due to accidental causes, but there is little or no direct clinical evidence to show that any deaths are due to overdosage.

We may now consider the mode of death in these cases. It will perhaps carry more conviction if I quoted the words of Snow in commenting upon a number of cases (44) collected by himself, all of which are included in my table. He says[13] "In all cases in which the symptoms which occurred at the time of death are reported, there is every reason to conclude, as shown above, that death took place by cardiac syncope, or arrest of the action of the heart. In forty of these cases *the symptoms of danger appeared to rise entirely from cardiac syncope*, and were not complicated by the over-action of the chloroform on the brain. It was only in four cases that the breathing appeared to be embarrassed and arrested by the effect of the chloroform on the brain and medulla oblangata, at the time when the action of the heart was arrested by it, and only in one of these cases (No. 42 or No. 50 in the Med. Chi. Soc'y. list) that the breathing was distinctly arrested by the effect of the chloroform, a few seconds before that agent also arrested the action of the heart."

These are Snow's words. The theoretical conclusions he arrives at are not material to the question under consideration; but I have dealt with them in the appendix; and I would point out that the remaining cases in the list might be summarized in almost precisely similar words, for death is clearly described in the great majority of cases as occurring by primary cardiac syncope. This mode of death confirms with my theory of death by ventricular fibrillation, and all the clinical symptoms and manifestations of this form of syncope are very fully illustrated in many of the reports. A reference to the original reports will confirm this statement. One example has already been reproduced in full. The symptoms correspond to the adrenalin death, which is without a scintilla of doubt due to ventricular fibrillation. A further report of a fatality taken almost at random from more recent literature, is likewise illustrative.

ILLUSTRATIVE CASE: Woman, aged 40. Pale and thin. Anesthetic, chloroform, 2 drachms; a little ether added towards end of induction. Induction gradual, by drops on open mask, held all the time about an inch from the face. Some slight irritative coughing at first in spite of very gradual administration. This ceased and there were slight muscular movements of the limbs and a little muttering; no struggling. Respiration quiet and regular. Lips and ears very good color. Pupils medium, corneal reflex brisk. Then sudden alteration in breathing (five minutes after beginning of induction). There were seven or eight deep sighing respirations, and at the same moment wide dilatation of the pupil, pulse disappeared, no pallor for ten or fifteen seconds. Then cessation of respiration (no respiratory embarrassment at all before the sudden collapse). Tongue pulled forward, artificial respiration, oxygen, strychnine. No further sign of life.

The symptoms came on a very few seconds after a fairly brisk corneal reflex had been obtained, only a few drops had been added, the mask was always a little off the face." (Proc. Roy. Soc. of Medicine, Vol. V, No. 2).

Judging by the final remarks death would appear to have been due to a reapplication, only a few drops, probably, (and this can only be surmised) after an intermission; the description of method is of the usual vague nature. The degree of anesthesia was carefully noted; it was of a light description and the mode of death from primary cardiac failure is evident. There can be no other explanation of this death but that of ventricular fibrillation.

It is remarkable that for so many years a thin film of dogma has obscured our judgment of the conditions appertaining to death under chloroform. Physiologists have observed the patent fact that chloroform will kill if administered in sufficient quantity and for a sufficiently long time; therefore the word has gone forth that all deaths under chloroform are due to overdosage. Clinicians have resolutely read into every report of a fatality a possible (in many cases we may say an *impossible*) factor of overdosage and have shut their eyes to every other interpretation. At a touch almost, this obscuring dogma disappears, and to the logical mind the overwhelming evidence of light anesthesia favoring death stands revealed in glaring relief. How much simpler it is to accept this view than to strain the reports into an opposite interpretation!

When once these facts are grasped, the theory of death by overdosage perforce assumes a secondary position, and it remains to be demonstrated by clinical evidences that any deaths ever occur in practice from overdosage, my own impression being that few, if any, are so conditioned. Of course, overdosing is common enough in practice, and, admitting that the overdosed patient, with his heart's action and respiration seriously depressed, may be in a critical condition, yet I cannot conceive any qualified medical man guilty of bringing his patients into such a profoundly overdosed condition and delaying restorative measures so long that recovery becomes impossible.

For the safe administration of chloroform it is necessary to assuage the *fear of overdose* which has been fostered by extremists, and which has led to the exercise of an excessive caution in its administration. Under such circumstances there may arise a condition favorable to the onset of ventricular fibrillation, and consequent death. Provided that the vapor is administered in *fully sufficient concentration* and that it is administered *continuously*, I hold that there need be no fear of a fatal termination.

PRACTICAL CONSIDERATIONS.

It must now be admitted in view of the foregoing experimental and clinical evidence that the subject of light chloroform anesthesia requires very serious attention, and that appropriate precautions should be adopted. Fortunately these are very simple; the first principles are to keep the patient *fully anesthetized* and to make the *administration continuous*. I do not in any way advocate an excessive administration, for profound narcosis is uncalled for except by the exigencies of some special operations only; it can, and should be, avoided.

In the induction stage the administration should not only be continuous but should also be progressive; the strength of vapor should be increased as rapidly as is possible without distressing the patient, for it is well to bring the patient under the full influence of chloroform as quickly as is practicable. Sufficient vapor should always be available; to speak in percentage terms, a vapor of 3.5 to 4 per cent. strength may be required for exceptional and insusceptible cases, for such insusceptible cases always present elements of danger from imperfect anesthesia. In my opinion and experience a 4 per cent. vapor strength may be used with impunity when attained in progress-

ive stages, but it should not be used for long, and it should not be used unless necessary. For some cases a 2 per cent. vapor is sufficient, but these cases are in a minority.[14] Should the patient become excited or struggle during the induction, the administration should never, on any account, be remitted, as is at present the practice and teaching.

There is one practical detail which I believe is important, and that is to keep the patient entirely undisturbed until fully under the anesthetic. It is too frequent a practice to attempt to save time by scrubbing or shaving the skin during the period of induction; this may produce excitement, and, therefore, even the bandages should be left undisturbed until consciousness is absolutely abolished.

The skin incision and the earliest stages of the operation should be performed under a full degree of anesthesia, with the pupils slightly dilated and with a faint corneal reflex only. The strength of the vapor may be diminished as the operation proceeds, for then a lower percentage suffices to maintain a sufficient depth of narcosis, but all severe operative procedures should be anticipated by a more liberal administration.

These new facts which I have presented almost appear to reopen the old and oft debated question—whether to watch the pulse or the respiration. There can be no doubt that both pulse and respiration should receive attention, and the respiration the greater share. No process of inhalation can be successful without a properly maintained respiratory process, and further, weakening of the respirations remains the most important sign of impending excessive dosage. The pulse should unquestionably be kept under observation likewise, for any of the abnormalities of the heart-beat to which I have already referred (either single dropped beats or more complicated irregularities) may provide danger signals of important significance; at the same time one cannot rely on the pulse as a guide to underdosage, as one can on the respiration as a guide to overdosage; for an irregular pulse may be followed by ventricular fibrillation with startling rapidity, and the time all too short to adopt remedial measures.

I feel constrained to touch upon a certain condition which is not uncommon and which is dangerous. The patient is not overdosed, a fair corneal reflex is present, the pupils are somewhat dilated, the skin pale and sweating; the pulse is rapid and small. This condition is the result of sympathetic reflexes from sensory stimuli; it is generally regarded as one of shock, but it is not so in the proper sense of the word, for the blood-pressure may be well sustained. Should the anesthetic be remitted during this condition a disaster *might* occur; the interests of the patient would be best considered by stopping the operation for a little while and putting him more deeply under the anesthetic before proceeding further.

Narcosis should be properly maintained up to the last stages of the operation; and after short operations even during the final bandaging. Never try to rouse the patient, but when everything is completed get him put back to bed with as little disturbance as possible. For short operations chloroform should be very fully administered, for cardiac syncope may occur during the rapid recovery which follows a brief and light administration of chloroform. In the case of children, the danger is probably less, for they do not appear to be so subject to this form of syncope as are adults, but it is well even in their case to ensure very full anesthesia before discontinuing the administration.

To attain a continuous administration a methodical procedure is obviously desirable; probably the nature of the method is not so important as the employment of *some* method, whether by inhaler or otherwise. Every expert anesthetist has doubtless by dint of experience developed his own method, but the uninitiated may find some hints on methodical procedure with the simplest appliances in a former paper which I have published appertaining to the physical conditions of the evaporation of chloroform.[15] I have found it possible not only to develop methods with simple appliances, but what is more important, to make them teachable to students.

It has been shown how the most constant conditions are attained when breathing *through* a previous fabric. The strength of the vapor may then be effectively controlled by moistening successive circumscribed areas of the fabric. A drop method is employed,

and it is advisable to control the applications according to the rate of breathing.

It is not every error of administration that is penalized by death of the patient, as you will have gathered from my experiments on animals, and it is a fortunate circumstance that men are not so liable to ventricular fibrillation as are cats; but a repetition of errors of the kind I have mentioned in detail will inevitably exact its toll of fatalities.

I have entered into the particulars in some detail; they are perhaps a counsel of perfection, for the essential points are merely *full and continuous anesthesia*. The first of these points was insisted on by Syme in the old Edinburgh days and practiced with undoubted success; the second is no less important. There is no doubt that under Syme's instructions his patients were fully anesthetized, and according to Lister he never had a death from chloroform to the end of his career. This fact not only supports my views in regard to the danger of light anesthesia, but it likewise confirms my contention that there is very little if any real danger of death by overdosage in the hands of fairly competent administrators, and it must be remembered in this connection that Syme's anesthetics were given by his house surgeons, and not by specially trained anesthetists; in fact, although some degree of overdosage is a common enough event in practice, I do not think any qualified anesthetist is likely to push the process to such an extreme degree that the vital functions become extinguished beyond all hope of resuscitation.

It is now obvious that the present-day teaching, that safety lies in the attention of vapor percentages, must be permanently abandoned, but there is no reason for a violent reaction, leading to the adoption of the extreme opposite practice. Excessive dosage is of course undesirable in every way, apart from the immediate question of danger to life, and it may be avoided most readily by the same practice which I have already advocated as tending in part to avoid death by ventricular fibrillation by a methodically controlled and continuous administration of vapor; in other words, by maintaining a steady level of anesthesia, so far as the exigencies of the operation will allow.

What are the proper methods of resuscitation to adopt when ventricular fibrillation is established? The only remedy, so far effective, is massage of the ventricles. It is not advisable to attempt this at once, for the heart may recover spontaneously; two minutes' grace is all I would advise. During this interval I would continue to keep the lungs well charged with vapor by artificial respiration in anticipation of a tendency to relapse after recovery. At the end of two minutes, if there is still no indication of cardiac action, open the abdomen, and with the hand compress the ventricles between the diaphragm and the chest forcibly and rhythmically. Artificial respiration should be maintained meanwhile, so that the heart may not die from asphyxia, for a measure of circulation is maintained by the cardiac compression. Undoubtedly direct digital compression of the ventricles would be the best measure to adopt to restore the heart's functions; it is generally successful in animals after a time, but it could only be attempted in the human subject if proper means were available for insufflating the lungs after opening the thorax; whether such an extreme measure would result in permanent recovery of the human patient can only be told from actual experience.

I may here introduce a few words regarding the much discussed relation of asphyxia to sudden death. I investigated this subject experimentally some time ago, and was then quite unable to confirm any relationship, short of complete suffocation,[16] but I now find the irregularities induced by asphyxia under light chloroform anesthesia may, as an exceedingly rare event, proceed to actual fibrillation, as I have indeed observed in a single and non-fatal instance. Danger is more likely to arise in practice if the chloroform be withdrawn after the airway has been cleared, and the patient is recovering from profound asphyxia. That the danger of asphyxia under chloroform has been greatly exaggerated is evident from a consideration of the Medico-Chirurgical Report, for in four cases only is there any reference to a dusky complexion preceding death; in each case there was other sufficient reason for death occurring, and it is an open question, on clinical evidence alone, whether the asphyxia had any relation in this respect.

A word of warning in regard to the use

of atropin. This throws the vagi out of action, and no doubt favors ventricular fibrillation under light anesthesia; in fact, it will frequently cause death under such conditions when injected into a vein in animals. When very deep anesthesia is required it is probable that atropin sustains the heart's action, and it should only be employed under such circumstances, otherwise I regard its use as inadvisable.

As a final point of clinical interest I may add that the drugs known as epenine, epinephrin, tyraminal and suprarenin, act precisely like adrenalin, but I cannot find any definite objection to the use of pituitary extract for the treatment of shock under chloroform; this substance is a cardiac stimulant to a slight degree, and should, therefore, be used with some caution, but I have not succeeded in causing death in cats by its agency.

CONCLUSIONS.

The theory of death by overdose has, in my opinion, been a most deplorable one for humanity; it is, I believe, the most unfortunate theory to which physiological science has ever set the impress of currency. I would urge upon those who still continue to lay exaggerated stress upon the risk of death by overdosage that they assume a grave public responsibility in regard to the perpetuation of chloroform fatalities.

APPENDIX.

In considering the theory of death by overdosage we must go back to the researches of John Snow, because the problem has remained largely as he left it, and because he made important observations which have become obscured in the swirl of subsequent controversies. His observations fall under two headings:

(*a*) *Clinical;* he concluded definitely that, in man, death under chloroform was signalized by a stoppage of the heart while the respirations were yet unimpaired—an instantaneous event occurring without warning. This conclusion is of the first importance, but it has become slurred over and ultimately lost sight of by subsequent writers; and why? Because up to the present moment no experimental observations have ever been made either by Snow or any one else which afford a satisfactory explanation of it.

(*b*) *Experimental;* he found that by administering chloroform vapor to animals in any concentration up to 6 per cent. for a sufficient period of time the respirations were first depressed and then ceased, and the heart failure, which was gradual and never sudden, was a subsequent event to the respiratory failure. He likewise pointed out that in reported cases of death under chloroform in man, in no case had it occurred in this gradual sequence.

Snow's attempt to investigate the clinical condition of death which he recognized, namely—sudden cardiac syncope—forms the least convincing portion of his experimental work, but briefly his conclusions amount to this—that vapors of 8 to 10 per cent. value may cause sudden stoppage of the heart, but vapors of 6 per cent. and under do not do so, and therefore are not responsible for fatalities. I have already pointed out the fallacy of the few experiments which Snow performed with the higher percentages elsewhere, but they need not detain us, for we know that vapors of 8 to 10 per cent. value are outside the range of percentages available with the ordinary appliances in clinical use, on account of the difficulty of obtaining a stronger vapor than 4 per cent. from an ordinary mark, and we are therefore driven to conclude that Snow never did, as he is generally credited with doing, provide a satisfactory explanation of death occurring in the course of the administration of chloroform. However, the general result of Snow's researches has been that death under chloroform in man has been ascribed to overdosage, although, with the exception of Embley's work, no subsequent evidence has been adduced to make the position any more satisfactory. The strength of vapor which Snow deemed it advisable not to exceed for clinical purposes was 4 per cent., but deaths continued despite mechanical control of the vapor to this limit. Later on Paul Bert and his school narrowed the limit down to 2 per cent., and this percentage was declared sufficient for all purposes. Bert's teaching was strongly insisted upon by a more recent Committee of the British Medical Association, but deaths still continue and multiply; in fact, the more the limitation of chloroform vapor is insisted upon, the more frequent do chloroform fatalities become.

Later physiological research has mainly centered around the mechanism by which life is suppressed in conditions of deliberate overdosage, but little of outstanding scientific value became added to our knowledge until Embley, working on fresh lines, adduced a fact of some apparent importance. He showed that in dogs a primary cardiac failure might occur resulting from vagal inhibition of the heart as a result of the direct excitation of the vagal centres by an excess of chloroform. Embley, I think, overrated the importance of his discovery, owing to the unrestricted use of morphin in addition to chloroform; a very strong vapor is evidently requisite to produce this reaction in non-morphinized dogs—strong enough, in fact to reduce the blood pressure very rapidly, and evidently stronger than anything employed in ordinary clinical routine. Moreover, Embley neglected to study the effect of artificial respiration in relation to recovery of his inhibited hearts, and this is the more important because there exists evidence of a strong tendency towards spontaneous recovery after inhibition. Furthermore, Embley's theory would account for death during the induction period of anesthesia alone, for the vagal inhibition does not occur in the later stages of anesthesia, and it is therefore limited in application.

More recently Yandel Henderson has strongly urged that *acapnia* should be considered a determining factor in death under chloroform. This essentially involves a

death by respiratory failure, a phenomena which is only on very rare occasions *even suggested* by reports of fatalities. Henderson's suggestion that acapnia may account for sudden cardiac failure goes far beyond the warrant of his experimental work. It is noteworthy that Henderson lays great stress on the fact that animals die under light anesthesia, but it is generally felt that his theory has not been fully established.

There is in fact no theory that gives so complete and satisfactory an explanation of that dreaded catastrophe,—death under chloroform, as that which I have advanced, and which has recently been confirmed in its essential details by Prof. J. W. McWilliams,[37] one of the earliest students of the condition known as *Ventricular Fibrillation.*

ANALYSIS OF 109 CASES OF DEATH UNDER CHLOROFORM, COLLECTED BY THE CHLOROFORM COMMITTEE OF THE ROYAL MEDICAL AND CHIRURGICAL SOCIETY, PUBLISHED IN 1864.

Cases excluded on account of complete lack of detail. Total 11.

Nos. 6, 9, 15, 23, 60, 65, 67, 77, 89, 91, 109.

Cases described by the Committee as not fully anesthetized. Total 47.

Nos. 1, 3, 4, 5, 7, 8, 11, 13, 16, 17, 20, 22, 24, 28, 30, 33, 34, 38, 40, 45, 46, 49, 52, 53, 54, 55, 56, 59, 61, 62, 63, 66, 69, 72, 73, 74, 83, 84, 90, 92, 93, 100, 101, 102, 103, 107, 108.

Cases showing definite evidence of light anesthesia, but not so described by the Committee.

No. 2. Inhalation one minute only; chloroform removed during operation for tooth extraction; groaned during the operation.

No. 14. Chloroform removed, toe-nail evulsed, struggled for one minute and then died; about ½ dr. of chloroform in an inhaler.

No. 19. The towel was removed, but the patient not being insensible it was applied again; after a few inspirations the pulse ceased and the patient died.

No. 29. "To prevent his becoming altogether sensible I commenced to give him a little more chloroform; he had only taken two or three inspirations when his breathing ceased." (Snow: On Anesthetics, p. 208).

No. 32. "Insensibility was not complete, for after the first incision was made the man more than once said a cat was scratching him." (Lancet, 1853, Vol. I, p. 21).

No. 37. The chloroform was removed while patient was still violent; having quieted down he was pulled into position and the perineum shaved; he died suddenly without having had any more chloroform.

No. 58. As soon as the patient became unconscious the inhaler was removed and acid applied to the warts; she moved her legs as though recovering from the anesthetic, and died a few minutes later; 1 dr. of chloroform in the inhaler.

No. 78. Chloroform given to relieve maniacial excitement; "great excitement and struggling."

No. 81. Operation ended, chloroform removed; a moan was heard; patient died.

No. 87. Chloroform reapplied; stertor appeared while struggling continued; sponge at once withdrawn; in another minute full stertor came on; pulse ceased; respiration continued for some time.

No. 95. "He suddenly raised himself in bed and the breathing ceased."

No. 96. Operation commenced; patient slightly conscious; another drachm of chloroform was applied, patient took one inspiration and pulse stopped.

No. 99. The patient moved his limb slightly and more chloroform was applied, when he suddenly became deathly pale and his pulse ceased.

No. 106. Seated in a chair; in three or four minutes "the spasm which precedes the loss of sensibility set in," when the pupils suddenly dilated, and no pulse could be felt.

Total 14.

Cases in which overdosage can be excluded.

No. 18. Death occurred suddenly after the administration was discontinued; 1 dr. of chloroform on a handkerchief.

No. 25. Induction with 70 minims of chloroform in about seven minutes; insensibility being established the further administration of chloroform was desisted from; the respirations were then unembarrassed, the pulse regular and about 70, the lips florid; the scrotum was then incised, blood flowed freely at the first, then almost instantly ceased; the pulse ceased at the same moment.

No. 26. Chloroform removed, pupil contracted, conjunctiva slightly red; operation performed without further chloroform; at end patient found to be dead.

No. 31. Caustic applied when insufficiently insensible, a little more chloroform given; caustic again applied without further chloroform; death on completion of application of caustic.

No. 35. Trismus preceded cardiac failure; death after less than five minutes' inhalation.

No. 36. One drachm of chloroform inhaled from a sponge held over the nose, the mouth being left free; the patient died on the first incision after inhaling in this way for four minutes only.

No. 39. The inhaler was removed and patient drawn into (lithotomy?) position, when the pulse was noted to be weak and fluttering, the pupils of medium size; the respirations gradually ceased.

No. 41. Operation for lipoma of the back; patient sitting up; 1 dr. of chloroform given; the patient fell forward on the incision being made and was found to be dead.

No. 42. One drachm of chloroform inhaled from a sponge for five minutes; a second drachm was then added, when the pulse stopped almost immediately after, the pupils were not dilated before death.

No. 43. "Symptoms of anesthesia," were obtained after two minutes' inhalation with considerable struggling; patient then drawn to side of bed and an assistant directed to put "several drops of chloroform on the compress," pulse ceased suddenly on performing a short operation; breathing continued; the compress had been removed several seconds before the pulse failed.

No. 44. Chloroform administered with "more than usual precaution," forty minutes taken to induce "conclusive signs of the satisfactory action of the chloroform," the pulse stopped suddenly just before the operation was commenced.

No. 47. Pulse failed suddenly on reduction of dislocation; the respiration continued; during a temporary recovery of the heart the patient extended his arms, and appeared to reply to questions; secondary collapse then occurred and death.

No. 51. Duration of inhalation about three minutes, "insensibility just fully established," when the pulse failed suddenly; 2 dr. of chloroform on lint.

No. 57. Patient partially recovered after two minutes without chloroform; another half drachm poured on lint and applied to nostrils, which was said to produce full anesthesia; respirations well sustained; pulse frequent and feeble; chloroform again taken away, after which pulse ceased and respiration shortly after; operation not begun.

No. 68. After operation; chloroform had been re-

moved; pulse and respiration regular; pulse stopped suddenly a little later.

No. 71. Inhaler removed, and then incision made; pulse fluttered and ceased; 1½ dr. of chloroform in inhaler.

No. 75. Dislocation reduced; chloroform removed; face became congested; respiration failed and stopped; no pulse.

No. 80. Chloroform wholly suspended, "when excitement subsided;" orbicular reacted distinctly, though sluggish; pulse full and regular; death while arranging patient in position.

No. 82. One drachm of chloroform in inhaler; death on commencement of operation.

No. 85. Sudden syncope two minutes after removing the chloroform while introducing a catheter.

No. 88. Sudden pallor and death at least two minutes after removing inhaler.

No. 94. Administration stopped after four minutes' inhalation; pulse ceased twenty seconds later, respirations continued.

No. 97. One and a half drachms of chloroform administered "with great precaution," in an inhaler; death twenty minutes from commencement; operation completed.

No. 105. Operation for fistula begun and completed after cessation of administration; breathing ceased three minutes later.

Total 24.

Cases in which overdosage was improbable. Total 6.

Nos. 10, 21, 27, 48, 64. 104.

Cases in which no opinion can be expressed as to the depth of anesthesia. Total 7.

Nos. 12, 50, 70, 76, 79, 86, 98.

Grand Total 109.

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THE TECHNICAL ABILITY TO SKILLFULLY ADMINISTER ANESTHESIA IS BY NO MEANS THE GREATEST ASSET OF THE EXPERT ANESTHETIST; AND THE ANESTHETIST OF WHOM NOTHING MORE IS REQUIRED, WHOSE JUDGMENT, IDEAS AND OPINIONS ARE NOT SOUGHT, BECOMES A MERE AUTOMATON. SUCH ROUTINE DRUDGERY, IN THESE DAYS OF REFINEMENTS IN ANESTHESIA, DOES NOT APPEAL TO THE TYPE OF MAN WHO HAS THE MAKINGS OF AN EXPERT AND WHO SHOULD BE ENCOURAGED TO DEVELOP ANESTHESIA INTO A FULL-FLEDGED SPECIALTY.

—William Hamilton Long.

LATE CHLOROFORM POISONING . TISSUE CHANGES INDUCED BY THE ADMINISTRATION OF HYDROCHLORIC ACID . NECROSIS-PRODUCING POWER OF CHLOROFORM SUBSTITUTION PRODUCTS . THE INHIBITING EFFECT OF ALKALI . IODOFORM AND BROMOFORM . LIVER NECROSIS AS AN EFFECT COMMON TO ALIPHATIC ALKYL HALIDES . CHLORAL HYDRATE LESIONS . GENERAL DISCUSSION . SUMMARY

BY EVARTS A. GRAHAM, M. D. *MASON CITY, IOWA.*

IT IS WELL KNOWN that the prolonged administration of chloroform may be followed by certain well marked morphological changes in the tissues, most conspicuous of which are edema, fat infiltration, multiple hemorrhages and necrosis of the central portion of the liver lobule. These changes have been extensively studied and excellent bibliographies may be found in articles by Bevan and Favil,[1] Wells,[2] Whipple and Sparry,[3] Howland and Richards,[4] and others. However, in spite of the large amount of study that has been devoted to the lesions, there has been little effort to analyze the factors involved in their production. At the present time there is no adequate explanation of how these changes are produced. A satisfactory explanation would be important not merely in connection with the action of chloroform itself, but rather because of the light which it would throw on the nature of the fundamental processes involved, which without doubt are identical with those concerned in poisonings of the body with a large group of toxic substances, including other narcotics, arsenic, salvarsan, phosphorus, and probably most bacterial poisons. Evidence will be brought to show that in chloroform poisoning the liver necrosis is produced chiefly by the action of acid (largely probably by hydrochloric acid which is formed in the metabolic destruction of chloroform), and this ability to produce liver necrosis is a general property of alkyl halides, all of which probably yield halogen acids in their breakdown in the body. Reasons will also be brought in support of the view that the accompanying cloudy swelling, fat infiltration, hemorrhages, and edemas are also acid effects. These changes, however, are not limited to intoxications with substances which can split off mineral acids, but they may follow the administration of any substance that can cause tissue asphyxia with its attendant accumulation of organic acids.

The ease with which extensive liver necrosis is induced by a two or three hour narcosis with chloroform, and the failure to obtain it by a narcosis with ether of three or four times that duration, suggest strongly that this difference in the behavior of the two substances depends upon either a difference in molecular action or a difference in products formed during their breakdown.

When chemically pure choroform is exposed to the action of sunlight at room temperature it is oxidized to phosgene and hydrochloric acid. The end reaction may be expressed thus:

$$CHCl_3+O=COCl_2+HCl.$$

This oxidation occurs so easily that it has become necessary for manufacturers of chloroform for anesthetic purposes to add alcohol to it to prevent its decomposition. Baskerville has shown that the alcohol protects the chloroform because it is more easily oxidized than chloroform, and hence when, as in a stoppered bottle, there is only a limited amount of oxygen present, the alcohol uses all the available oxygen for its own oxidation.[5] Phosgene in the presence of water is decomposed into carbon

dioxid and two molecules of hydrochloric acid. This hydrolysis may be expressed thus:

$$COCl_2+HOH=CO_2+2HCl.$$

It is at once apparent, therefore, that if one molecule of choroform is oxidized in the presence of water, three molecules of hydrochloric acid may be formed. The liberation of such a strong inorganic acid in the tissues could very easily produce necrosis and other acid effects; and since three molecules of the acid are formed from each one of the choroform, it might easily be supposed that the oxidation of only a small amount of chloroform would suffice to produce a considerable effect on the tissues. Moreover, the well known facts that the liver is the organ which most strikingly manifests the choroform necrosis, and that this organ is also the site of a most active metabolism, harmonize well with this hydrochloric acid theory.

With these facts and considerations as the basis for departure, the hypothesis was subjected to a series of experimental tests which may be outlined as follows:

(1) A study was undertaken of the morphological changes induced by hydrochloric acid, with special reference to the liver. (2) Attempts were made to demonstrate free hydrochloric acid in the necrotic areas in the livers of animals poisoned with chloroform. (3) Observations were made on the relative necrosis-producing power of different chlorin substitution products of methane (dichlormethane, chloroform, and tetrachlormethane), which on theoretical grounds could be considered to yield different amounts of hydrochloric acid in their breakdown. (4) The inhibiting effect of alkali was studied. (5) Attempts were made to produce the typical picture of chloroform poisoning by other alkyl halides of the same type as chloroform, *viz.*, bromoform ($CHBr_3$) and iodoform (CHI_3) which might be expected to give analogous products in their breakdown, with, however, the liberation of hydrobromic acid and hydriodic acid, respectively, instead of hydrochloric acid. (6) Experiments were made to ascertain whether or not morphological effects like those produced by chloroform can also be induced by alkyl halides in general, and whether these substances are decomposed in the body in such a way that the corresponding halogen acid is liberated. (7) A comparative study of the lesions produced by chloral hydrate and chloroform was made, since the former substance yields practically no hydrochloric acid in its metabolic breakdown, although it contains the same number of chlorin atoms as chloroform.

EXPERIMENTAL.

THE TISSUE CHANGES INDUCED BY ADMINISTRATION OF HYDROCHLORIC ACID.

Oral and intraportal administrations of hydrochloric acid in suitable concentrations were followed by edema, hemorrhages, necrosis, and increased fat accumulation in the liver. When injected intraportally in dogs in relatively high concentrations (10 to 25 cubic centimeters of 0.5 (N/7) to 1 per cent. (N/3.5) solutions), hydrochloric acid produced extensive liver necrosis involving large areas of many lobules about equally. When given in lower concentrations (0.37 per cent.) (N/10), it produced edema and other degenerative changes as well as numerous subcapsular hemorrhages. The parenchymatous changes were most conspicuous at the periphery of each lobule. This was to be expected since, because of the arrangement of the blood supply, the periphery would be the first part of the lobule reached by the acid. The degenerative changes consisted of pycnosis and fragmentation of the nuclei with swelling of the cells. It was felt that these were precursors of necrosis. When several administrations were given by mouth to rabbits in concentrations of 1 (N/3.5) or 2 per cent. (N/18) at intervals of from twelve to twenty-four hours, the animals usually died after the third or fourth administration. They showed extensive hemorrhage in the mucosa of the stomach and duodenum, large fatty livers, and swollen kidneys.

Microscopically, by the use of Sudan III, the fat in the liver was found chiefly around the central veins. In short, all of the marked morphological changes induced by chloroform have been seen to follow the administration of hydrochloric acid alone. They were, however, differently distributed. The liver necrosis appeared at the peripheries of the lobules instead of at the centers, as in chloroform poisoning, but this difference in location is not regarded as important, since a discusson of the site of the necrosis in chloroform poisoning involves the question of the site of the greater formation of hydrochloric acid together with that of the relative susceptibility of the central and

peripheral parts of the lobule to its effects. These points will be further elaborated in the discussion.

The production of fatty changes in the liver by the use of hydrochloric acid is in harmony with a statement of Leathes, that as an effect of "*the action of mineral acids an active mobilization of the fat reserves may occur . . and the liver cells are found loaded with fat of a low iodin value.*" Whether or not this mobilization of fat is to be considered as due to a primary effect of the acid or to the cellular asphyxia induced by the acid will not be discussed in this paper.

The extensive edema which follows the administration of hydrochloric acid confirms the well known observations of Fischer on the inhibition of water by tissue colloids under the influence of acids generally. The production of hemorrhages harmonizes with the frequency of their occurrence after tissue asphyxia, with its attendant formation of acid. Dovon[7] and his pupils first (1905-1906) called attention to the probability that fibrinogen is formed mainly in the liver and that the interference with normal liver function induces a diminished coagulability of the blood, a conclusion which later was confirmed by Whipple and Hurwitz.[8] In a previous paper in which it was shown that the various hemorrhagic diseases of the newly born are probably expressions of an asphyxial process,[9] we stated that this hemorrhagic tendency might be due to a "*more fundamental and wide-spread change, as a result of which not only fibrinogen, but innumerable other proteins tend to remain in solution or to pass into solution, with the result that apart from diminished blood coagulability there is a great reduction in the firmness of the vessel walls.*" Typical protocols follow:

Experiment 1.—Normal dog, weighing 5 kilos. 2.00 p. m. Under ether anesthesia abdomen opened and 2 cc. N|10 (0.37 per cent.) hydrochloric acid injected into radicle of portal vein (branch of superior mesentric). Marked dyspnea and muscular spasms occurred two minutes later. 2.30 p. m. 2 cc. again injected, followed by same symptoms. 2.45 p. m. Another injection of 2 cc. Few small hemorrhages noted on surface of liver. 3.00 p. m. Another injection of 2 cc. Hemorrhages more numerous; also appearing on wall of stomach. When liver is stroked with handle of scalpel a line is marked which immediately becomes dark red (as if hemorrhagic). 3.30 p. m. After another injection of 2 cc., marked respiratory spasm occurred with muscles of chest rigid. Artificial respiration necessary. Hemorrhages increasing. Stomach greatly distended. 4.00 p. m. Another injection of 2 cc. 5.00 p. m. Dog died. Stomach enormously distended with gas. Wall very hemorrhagic. About 10 cc. of unclotted blood in abdomen. On cutting the small vessels there is little tendency of the blood to coagulate. Several subcapsular hemorrhages on the surface of the liver were noted, varying from pin-head to 4 or 5 mm. in size. No gross increase in liver fat.

Experiment 2.—Dec. 23, 11.30 a. m. Two adult rabbits each given 50 cc. of 2 per cent. hydrochloric acid by stomach tube. Marked dyspnea followed. The same amounts of acid were given again on Dec. 26, Jan. 4, Jan. 10, and Jan. 15.

Jan 16. One rabbit was found dead in the morning.

Autopsy—The liver was large and yellowish, with very distinctive lobular markings. Frozen sections stained with Sudan III showed very extensive fat accumulation, most marked around the central veins. Kidneys were swollen and pale brown. Microscopically they showed marked parenchymatous degenerative changes, especially marked in the convoluted tubules. A few casts were evident.

Jan. 16. 1.30 p. m. The other rabbit was given the same amount of acid again. Dead at 4.30 p. m.

Autopsy—The liver was moderately fatty. The stomach and duodenum were markedly hemorrhagic; the duodenum was empty and firmly constricted throughout its whole length. The kidneys were swollen and pale.

ATTEMPTS TO RECOGNIZE HYDROCHLORIC ACID IN THE NECROTIC AREAS IN THE LIVER.

The practical identification of free hydrochloric acid depends upon the recognition of (1) free hydrogen ions and (2) free chlorin ions. It is obvious then that efforts aiming at the direct proof of the presence of hydrochloric acid in the tissues are necessarily complicated by the fact that both ions are always present. Therefore, at best, only circumstantial evidence can be brought to show the presence of free hydrochloric acid. However, the following observations were made.

It is possible to show a high hydrogen ion content in the central, necrotic portions of the liver lobules if fresh unstained sections are treated with indicators which do not change when placed in contact with equally fresh normal tissues in the same way. In this work most of the observations were made with neutral red and phenylated Nile blue. In every case the reaction between the indicator and tissue was much more marked in the central (necrotic) portion than at the periphery of the lobule. In some instances the tint assumed by the neutral red was a deep rose, approximating that which is obtained with a concentration of acid represented by $H+=10^{-6}$. Often the central portion was distinctly red, while the periphery was slightly yellowish. The Nile blue reactions were less satisfactory than those obtained with neutral red. If the area of necrosis was very marked, the response of the dye to the free hydrogen ion was shown by a definite blue color; but with moderate necrosis the color change often was insufficient to be satisfactory.

In order to minimize the formation of asphyxial organic acids during the time required to cut the sections and place them in contact with the indicators, the following method was used: Guinea pigs to which chloroform had been given two days previously for a period of four hours were again anesthetized with chloroform; and while unconscious the livers were removed. Sections were cut very quickly with a Valentine knife, washed in distilled water, and immersed in the dye on a slide. The whole process was some-

times done in less than one minute and always in less than two minutes. The neutral red was used as 1 per cent. aqueous solutions; alcoholic phenylated Nile blue was used in different concentrations, but generally of 1 or 2 per cent. strength.

In their work on the survival formation of lactic acid in amphibian muscle, Fletcher and Hopkins[10] have demonstrated that sarcolactic acid formation in frog muscles attains in maximum only after the lapse of hours, but in a much shorter time (thirty minutes) when the muscles after removal from the frogs are treated with chloroform vapor. In harmony with what is generally known concerning the action of narcotics during life there is no doubt that in choroform poisoning the asphyxial formaeion of lactic acid is great. The question has therefore to be met whether the indicator changes described in the preceding paragraph are actually greater than might be explained by the presence of much asphyxial organic acid. This objection to interpreting the dye reaction as indicative of the presence of an inorganic acid in the necrotic areas is recognized and has not been removed. In fact when pieces of excised normal liver are kept for six to seven hours at 37° C. in order to insure their maximal content of survival acid, such tissues react to neutral red with about the same intensity as fresh chloroform livers. It is clear from this that the cell itself has the power to produce enough acid during life to effect the indicator changes described. The experiments are merely recorded in conjunction with other observations.

For the determination of an excess of chlorin ion in the necrotic areas sections of liver were cut in the same way as above and handled in general according to the method used by Macallum and Menten.[11] They were placed in N|10 silver nitrate, containing 1.5 per cent. nitric acid, and kept in this bath, protected from the light for from twelve to twenty-four hours. They were then mounted in 50 per cent. glycerol and exposed to the sunlight until the maximum effect was produced. The most pronounced blackening always occurred in the central necrotic portions of the lobules. The peripheries of the lobules were light brown instead of black. In control sections of normal livers the darkening amounted to only a brownish discoloration resembling the tint of the periphery of the lobule in a chloroform liver. This discoloration has been extensively discussed by Macallum and Menten, who consider that in the tissues it is a definite indication of the presence of chlorides.

Although an excess of free H^+ and Cl^- ions in the necrotic areas of the liver was clearly shown, nevertheless this finding alone cannot be interpreted as in any way indicative of the presence of free hydrochloric acid. The possibility of other sources of hydrogen ion has already been mentioned. Recently Fischer[12] has shown that protein gels (fibrin) retain increased amounts of chlorides under the influence of acid. The excess of Cl^- ion in the necrotic areas, therefore, may represent only a greater accumulation or retention of neutral chlorides instead of hydrochloric acid.

As bearing on this point, however, it is of interest that the excretion of neutral inorganic chlorides in the urine is increased after the administration of chloroform, as has been shown by Zeller[13] and Kast.[14] Since hydrochloric acid formed in the tissues would doubtless be in part neutralized by metals in alkaline combination, this observation harmonizes with the present theory. Here also one must consider the possibility that an increased output of chlorides in the urine following administrations of chloroform may be due not so much to a splitting of the drug as to anomalies of metabolism and excretion set up in the process of narcosis. However, after the administration of iodoform there is, according to Mulzer,[15] an excretion in the urine of inorganic iodin indicative of a 60 per cent. splitting of the iodoform. This could scarcely come from the tissues; and by analogy it would seem probable that the increased chlorid excretion following chloroform administrations is due to decomposition of this drug. Moreover, after narcosis with chloral hydrate the urinary chlorides show no such increase as with chloroform.

NECROSIS-PRODUCING POWER OF OTHER CHLORIN SUBSTITUTION PRODUCTS OF METHANE.

A study of other chlorin substitution products of methane should be of interest from the standpoints of determining (1) whether they all have the power of producing central liver necrosis, and (2) whether this property is proportional to the number of molecules of hydrochloric acid which could theoretically be derived from them. If, starting with methane, we should outline a series of its various chlorin substitution products, we might expect, according to the theory, that those which could give the largest amounts of hydrochloric acid

in their breakdown would manifest the strongest tendency to produce the necrosis and other changes. Thus *a priori* we might expect the series to run in this order:

$$CH_3Cl < CH_2Cl_2 < CHCl_3 < CCl_4,$$

if all of these substances were equally broken down in the body. Experiments were carried out to determine this point. The last three of the series (CH_2Cl_2, $CHCl_3$, CCl_4) were selected as sufficient to test the tenability of this hypothesis. Reason for the assumption that tetrachlormethane might have greater necrosis-producing power than chloroform, and this in turn than dichlormethane lies in the fact that, in the ultimate breakdown of these substances outside of the body in the presence of water, four molecules of hydrochloric acid can be obtained from one of tetrachlormethane, three from chloroform, and two from dichlormethane. Thus Goldschmidt[16] has found that saponification of tetrachlormethane at 250° C. to take place as follows:

$$CCl_4 + H_2O = COCl_2 + 2HCl$$
$$COCl_2 + H_2O = CO_2 + 2HCl$$

The well known reactions by which three molecules of hydrochloric acid can be derived from chloroform, by simple oxidation in the presence of water, have already been discussed. Concerning the transformation of dichlormethane, André[17] has shown that in five hours at 180° C. 73 per cent. is decomposed as follows:

$$2CH_2Cl_2 + 2H_2O = 3HCl + CH_2O_2 + CH_3Cl$$
$$CH_3Cl + H_2O = HCl + CH_3OH$$

Thus from one molecule of dichlormethane two molecules of hydrochloric acid may be formed.

When these various substances were administered to animals by inhalation, it was found that not only did all three possess the power of producing central necrosis of the liver, but that this power was shown in greatest degree by tetrachlormethane, notwithstanding its higher boiling point, and least by dichlormethane, the most volatile of the three. In all respects the toxicity of tetrachlormethane was greatest, and that of dichlormethane least. A comparison of the minimum fatal doses of the three substances when given intravenously to rabbits again bore out the same relationship as by the inhalation method. The following table shows the minimum fatal doses:

Substance.	Mimimum fatal doses per kilo of rabbit.	Mimimum fatal doses expressed in gram-molecular concentrations.
CCl_4	0.053 gm.	0.000344
$CHCl_3$	0.085 gm.	0.000711
CH_2Cl_2	0.147 gm.	0.00161

The quantities injected were shaken up with enough water to make one cubic centimeter.

In other words, both the general toxicity of these substances as well as their power to produce the extensive morphological changes paralleled the amounts of hydrochloric acid which they can give in their respective breakdowns outside of the body. The toxicity of tetrachlormethane was so great that if it were administered by inhalation for two hours the animal almost invariably died within twenty-four hours. At autopsy numerous hemorrhages were present with extensive visceral edema, fatty changes, and beginning central liver necrosis. In a few instances the abdomen contained a large amount of free, unclotted blood. It was only by giving the tetrachlorid for about one hour or less that an animal could be expected to survive long enough to develop a well marked typical liver necrosis. As has been said above concerning chloroform, the most extensive necrosis is seen about two days after the administration of tetrachlormethane. A two hour narcosis with dichlormethane is usually not sufficient to induce an outspoken necrosis of the liver. A comparison of the narcotic properties showed that dichlormethane is less powerful than chloroform. With tetrachlormethane it was difficult to produce a quiet narcosis analogous to that accompanying the use of chloroform. More or less severe muscular spasms, particularly of the extremeties, occurred intermittently. This fact has already been noted by von Ley.[18]

The experiments were conducted as follows: Each of a series of three guinea pigs of approximately the same weight was placed under a bell jar, opened at the top to admit air. Into each jar was dropped enough of one of the three substances to induce narcosis, which was then carefully maintained at as nearly as possible the same depth and for the same length of time. Seven sets of animals were used; and the duration of the narcosis was varied from one and one-half to four hours. A typical protocol follows:

Guinea pigs A, B, and C, weighing respectively 550, 530 and 505 gm., were each put under a bell jar, as described above. To A was given dichlormethane; to B, chloroform; and to C, tetrachlormethane. These substances were administered for two hours. On the morning of the second day C was moribund; then all

three were killed by a sudden, overwhelming dose of chloroform. An autopsy C (tetrachlormethane) showed several pulmonary and subperitoneal hemorrhages; the liver was large and fatty; and the kidneys were swollen and gray. B (chloroform) showed no marked gross changes except a large, fatty liver. A (dichlormethane) had a moderate accumulation of fat in its liver; but otherwise there were no gross changes of importance. Microscopically the liver of C (tetrachlormethane) showed definite areas of necrosis which involved nearly the whole of the lobule in each case, but which nevertheless had apparently begun at the central portion of the lobule. This necrotic area of each lobule contained cells with fragmented nuclei; and there was a tendency for the whole area to stain intensely with eosin. There were no parenchymatous cells evident which contained normal-looking nuclei except at the periphery of the lobule. There was a large amount of infiltrated fat, as shown both by staining with Sudan III and by the presence of many fat vacuoles in sections prepared and stained in the ordinary way with hematoxylin and eosin. The cells of the kidneys were swollen and granular, and fat vacuoles could be made out here and there. Guinea pig B (chloroform) microscopically showed changes which differed from those of C only in degree. The liver contained areas of well marked central necrosis, which, however, involved only about one-fourth to one-third of the lobule. A (dichlormethane) showed no definite areas of liver necrosis at all comparable to the other guinea pigs. But about the central veins there were occasional necrotic cells and a conspicuous accumulation of fat. The typical necrosis, however, such as is seen after chloroform, was obtained with dichlormethane when it was administered to a guinea pig for from four to six hours.

THE INHIBITING EFFECT OF ALKALI

If the theory is correct that chloroform liver necrosis is an effect chiefly of acid, then it might be expected that the administration of an alkali simultaneously with the chloroform would inhibit, if not actually prevent, its occurrence. Such was found to be the case. When sodium carbonate was given intravenously in a proper concentration in a hypertonic solution of sodium chlorid, the liver necrosis was either entirely prevented or greatly inhibited. It was of course difficult to know in any given case how much alkali to administer as it was not possible to estimate how much acid was being formed. Moreover, it was obviously desirable to avoid an excess of alkali, since this in turn will give rise to some of the serious effects of an excess of acid, such as swelling of protein colloids, as shown by Fischer.[19] The amount of alkali given in each experiment was therefore decided empirically; and consequently the degree of inhibition of the necrosis was subject to wide variations in the different experiments. In only one instance, however, and that in the first experiment, was there a failure to observe a definite diminution of necrosis when alkali in hypertonic sodium chlorid solution was administered. In this one instance the dose of alkali was excessive (17 grams of $Na_2CO_3.10H_2O$ in 1,700 cubic centimeters of 1.4 per cent. sodium chlorid solution to a dog weighing twenty-one kilos, intravenously). Because of the onset, on the following day, of extreme thirst and a severe hemorrhagic nephritis, with passing of urine thick with blood, it was felt that clearly an overdose of the solution had been given. In all of six subsequent experiments, in which a much smaller dose was given, there was less necrosis than in the control animals which did not receive alkali. In one case no necrosis at all occurred. Another interesting fact was that in all of these six experiments the alkali animals seemed less toxic, and at autopsy other changes characteristic of chloroform poisoning, as well as the liver necrosis, were less conspicuous than in the control animals. This beneficial effort of the alkali was particularly striking in the kidneys. In the control animals, which received no alkali, these organs were always enormously swollen and weighed much more than those of the alkali animals. The effect of the alkaline hypertonic salt solution in inhibiting the swelling of these organs, tends to support Fischer's views on the nature and origin of edema. In only three of the experiments was the amount of visible fat in the alkali livers conspicuously less than in the controls. In none of the experiments was there noted any particular influence of the alkali either in strengthening or weakening the narcotic power of chloroform.

The alkaline solution used was that employed by Fischer in his work on edema; distilled water 1,000 cubic centimeters; Na_2CO_3-$10H_2O$, 10 grams; sodium chlorid, 14 grams. The method of conducting the experiments was as follows: The animals were always run in pairs; and the duration of the anesthesia was the same for both animals, as was also the depth of the narcosis, as nearly as could be determined. To one animal was given the alkaline solution and to the other was given the same quantity of a 0.85 per cent. sodium chlorid solution. Two sets of guinea pigs and four pairs of dogs were used, in all twelve animals, exclusive of the first pair already mentioned, in which clearly an excessive dose of alkali was given. The solutions were always injected into the blood stream. With the guinea pigs the injections were made by means of a syringe into the heart; but with the dogs, they were given by means of a cannula into either the saphe-

nous or femoral vein. The solutions were always warmed to body temperature previous to being injected; and the amounts were varied in different experiments. In general, the injections were made shortly after the animals had lost consciousness, and they were given slowly. Two days after the administration of the chloroform the animals were killed with chloroform and examined. Pieces of the various tissues were fixed in Zenker's fluid and 10 per cent. formalin and were stained both with hematoxylin and eosin and with Sudan III for fat. Typical protocols follow:

Experiment 3—Two adult dogs. A weighed 4.5 kilos; B, 5 kilos. Both dogs were given chloroform by inhalation for four and one-half hours. The chloroform used was Mallinckrodt's, *Purified for Anes-*

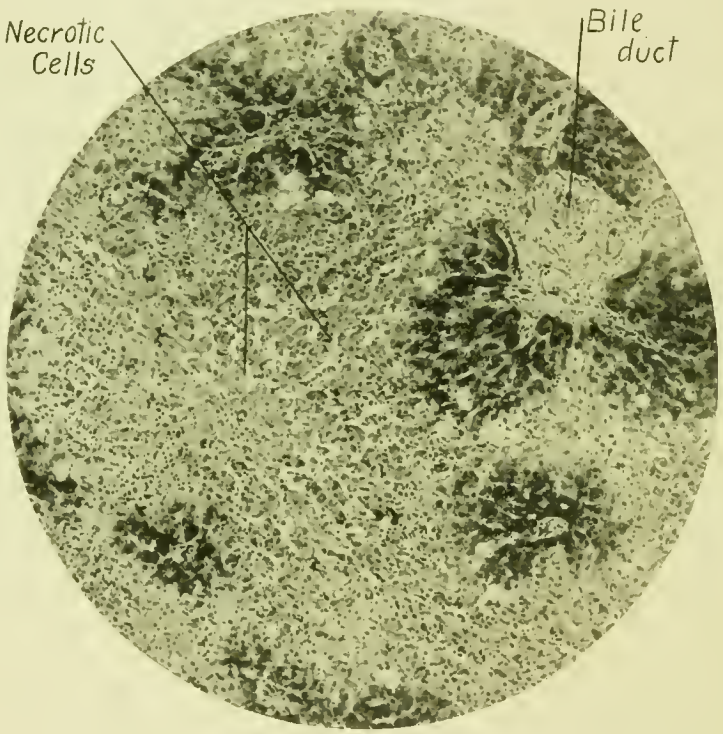

Figure 1. Typical central liver necrosis produced by chloroform anesthesia for four and one-half hours in Dog B of Experiment 3. Nearly all the lobule is affected. Microphotograph x83.

thesia. As soon as both dogs had lost consciousness cannulas were inserted into the saphenous vein; and into A were injected 150 cc. of the alkaline solution already described, and into B, 150 cc. of 0.85 per cent. sodium chlorid solution. Both solutions were injected slowly over a space of one hour. Both dogs were still in a condition of deep narcosis when they were returned to their cages at the close of the experiment. On the next day Dog A (alkali) was lively and playful; but Dog B (control) was exceedingly drowsy and difficult to arouse. Water and meat were allowed freely. On the second day after the experiment both dogs were killed with chloroform and examined. The difference between the two dogs was very striking. Dog B (the control) had a very fatty, yellowish liver. There was a large subperitoneal hemorrhage on the liver; and there were numerous ecchymoses on the parietal peritoneum. The kidneys were swollen and gray in appearance; and together they weighed 68 gm. Dog A (alkali), on the contrary, showed no hemorrhages. There was little, if any, less fat in its liver than in B's, but the kidneys were practically normal in appearance and weighed only 43 gm. This marked difference in weight between the kidneys of the two animals is particularly striking since the weight of the dogs before the experiment was practically the same. Of still greater interest, however, is the difference in the microscopical findings in the two animals. The liver of B (control) shows areas of necrosis so extensive that practically the entire lobule is involved. There is little more than a fringe of cells about the periphery which have not lost their nuclei. The necrotic areas stain deeply with eosin; and the only nuclei that can be distinguished are those of the capillaries and not of the parenchymatous cells. There are numerous fat vacuoles, especially in the peripheral portions of the lobules. The liver of A (alkali), however, shows practically no necrosis. Only an occasional necrotic cell about the central veins is evident. The columns of cells stand out plainly, and their nuclei appear to be unchanged. There is a moderate amount of fat accumulation about the central veins. These differences are well shown in the accompanying illustrations (Figures 1 to 4). The kidneys show also rather a marked difference, as might be expected from the striking difference in weight. The epithelium of the convoluted tubules in B's (control) kidney is swollen and granular, and it contains numer-

ous fat vacuoles. There are occasional casts. A's (alkali) kidneys show no striking changes. The changes in the other organs were relatively slight in both dogs.

Experiment 4—June 3, 1914. Two adult dogs: A, weighing 2.7 kilos; B, 2.5 kilos. Both dogs were given chloroform by inhalation for four and one-half hours. As soon as consciousness was lost A was given 80 cc. of the alkaline solution into the saphenous vein; and B was given the same amount of 0.85 sodium chlorid solution. Two days later both dogs were killed with chloroform and examined. Both livers were very fatty, but microscopically B (control) showed much more necrosis than A. The pictues were very similar to those described in the previous experiment. The kidneys here again showed a striking difference. Those of B (control) weighed 35 gm., and those of A (alkali) only 26 gm., although A was the larger dog.

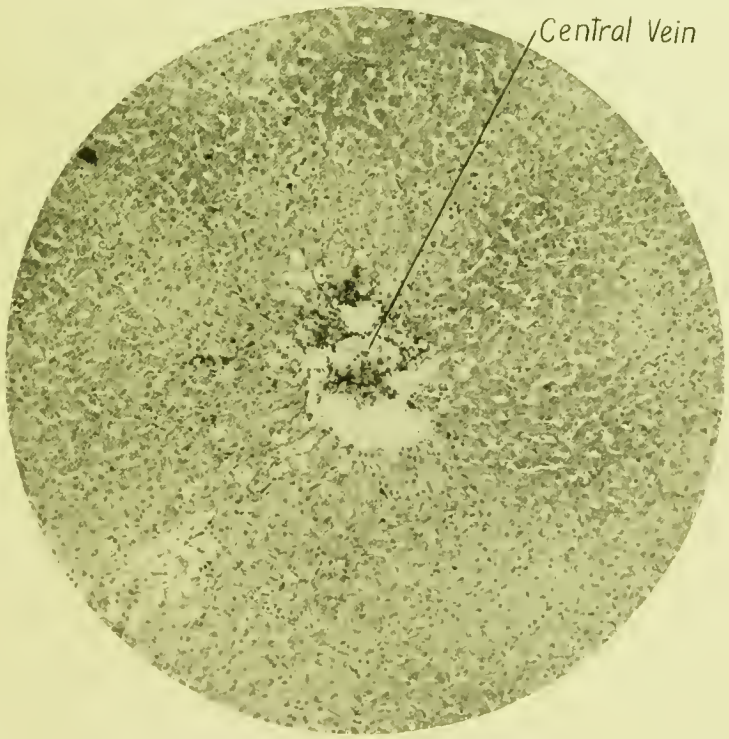

Figure 2 Inhibition of necrosis by the intravenous injection of 150 cc. of Fischer's alkaline, hypertonic salt solution, as shown in Dog A of Experiment 3, which had received chloroform for the same length of time as Dog B. There is practically no necrosis. Only a slight amount of fat accumulation in the cells about the central vein has occurred. Microphotograph x83.

In the two experiments on guinea pigs the method consisted of putting two guinea pigs of approximately the same weight under a large bell jar and dropping chloroform into it through an opening at the top. In this way it was assured that both guinea pigs were breathing air with the same concentration of chloroform. After losing consciousness the alkaline solution was injected into the heart of one of the guinea pigs; and the other guinea pig was given 0.85 per cent. sodium chlorid solution in the same way. Both were then returned to the bell jar, and the anesthesia was continued.

PRODUCTION OF TYPICAL CHLOROFORM LIVER BY IODOFORM AND BROMOFORM.

Iodoform (CHI_3) and bromoform ($CHBr_3$) are so similar to chloroform ($CHCl_3$) in chemical structure as to suggest that they might have a similar power to produce the characteristic morphological changes of chloroform poisoning. Here, however, we should of course be dealing with an effect of hydriodic acid and hydrobromic acid, respectively, instead of hydrochloric acid. As a matter of fact, not only do both of these substances induce lesions which are in every way identical with chloroform effects, but it is also possible to obtain some evidence that in each case the respective halogen acid is produced in the body. It has been known for some time that the administration of iodoform in large quantities is frequently followed by visceral fatty changes and multiple hemorrhages.[20] In our experiments we found, in addition to these changes,

a definite central liver necrosis in every way comparable to that produced by chloroform. Bromoform was found to produce identical changes. Evidence that here also we were dealing with an effect of acid was obtained by finding that the necrotic areas in the liver reacted to neutral red in the same manner as has been described already for chloroform. Attempts to identify iodin ions in these necrotic lesions failed, but iodin was found in large quantities in the urine. It is not altogether surprising that we failed to find it in the tissues, since it doubtless occurs in small quantities at most; and, furthermore, because of its tendency to combine with fats and protein, the body. The finding of iodides is an old observation. Thus Binz[21] in 1877 attributed the toxic action of iodoform to iodin, because of the presence of inorganic iodin in the urine. Hogyes,[22] Harnack and Grundler,[23] and Mulzer[24] have all concurred in this observation. Mulzer's study is especially interesting. He states that most of the urinary iodin is inorganic, in the form of alkali iodides and iodates. Of these, the iodides always appear first. Only about 60 per cent. of the calculated iodin can be found in the urine. The rest is eliminated into the sweat, hair, and intestines. Different structures of the body vary in their power to transform iodoform into inorganic iodin

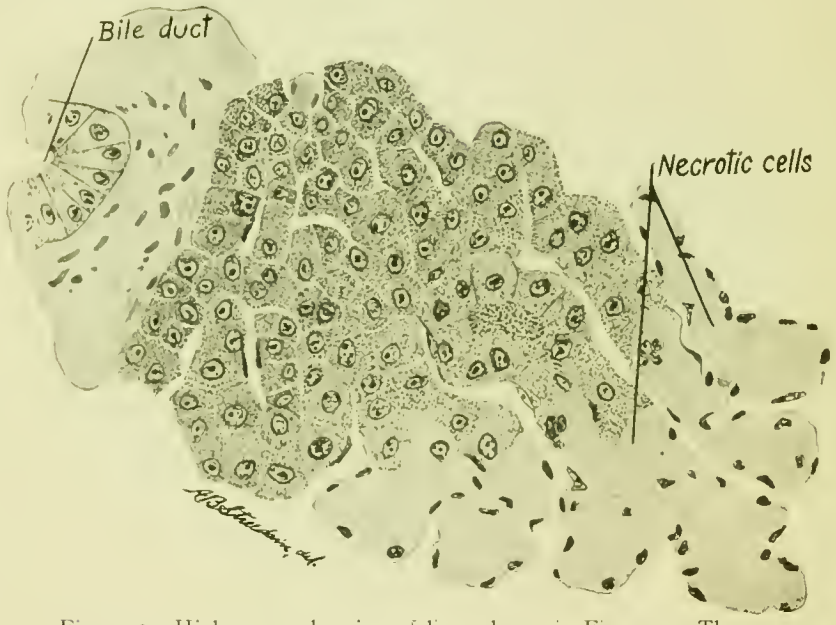

Figure 3. High power drawing of liver shown in Figure 1. The necrotic cells in the central portion of the lobule stain intensely with eosin. The nuclei of the parenchymatous cells have disappeared; and only those of the capillaries are evident. ×350.

probably nearly all of the iodin would be present in an organic, and hence non-ionic, form. The methods used for its identification will be described below. They were based on the standard means of identification of inorganic iodine by use of dilute sulphuric acid, sodium nitrite, and starch paste.

It is especially interesting that inorganic iodides may be found in large quantities in the urine after the administration of iodoform; for this necessarily implies the previous formation of hydriodic acid, at least somewhere in compounds. Muscle and liver hash seem to be the most powerful; and the muscle hash is a little more powerful than the liver. These findings are all in harmony with the idea which is being developed in this article; *that the decomposition of this group of drugs in the body is associated with the formation of the respective halogen acid, in this case hydriodic acid.* Furthermore, if we regard this decomposition as essentially dissociation in the presence of water, as we did in the case of chloroform, then we were not surprised that it occurs in

greatest quantity in the liver and muscle tissue where metabolic activity is greatest. The apparent discrepancy between Mulzer's and our own results, in that he found inorganic iodin in the liver where we failed to find it, is easily explained by the fact that he subjected relatively enormous quantities of iodoform to the action of the tissue hash and so obtained a recognizable amount of inorganic iodin which was not bound to protein. Even then his yields of iodin were small.

Figure 4. High power drawing of the liver shown in Figure 4. There is no appreciable necrosis, and only a moderate accumulation of fat has occurred in the parenchymatous cells and around the central vein. x350.

In our experiments with bromoform no attempt was made to find bromin ions. After demonstrating the identity of the morphological findings obtained with chloroform, iodoform, and bromoform, and recognizing that chloroform and iodoform may form in the body hydrochloric acid and hydriodic acid, respectively, the parallelism with bromoform was so close that this detail was omitted as unessential. Typical protocols follow:

Experiment 5—Adult dog, weighing 2.7 kilos. Injected daily subcutaneously with 2 gm. of iodoform (Merck), stirred up in 10 cc. of paraffin oil, for three days. On the third day when the injections were stopped, there was a strong reaction for inorganic iodin in the urine, as determined with starch paste. The dog had lost its appetite and had begun to look emaciated. On the sixth day (three days after stopping the injections) it was unable to stand, but, at intervals, while lying down, it would moan and howl feebly; and simultaneously there would occur frequent twitchings and cramp-like motions of the legs. At no time did the animal seem conscious of its surroundings. It refused meat and water; and between these times of activity it was drowsy and somewhat difficult to arouse. The strong reaction for iodin in the urine had persisted. The dog was killed with ether, but before death occurred a portion of the liver was removed and examined for free H^+ ions in the manner already described in connection with chloroform. The reactions to the indicators were less intense than was chloroform. Other liver sections were then treated for various periods for from one to thirty minutes with a little dilute sulphuric acid and sodium nitrite, later removed from this bath, and placed on slides. To the sections on the slide thin starch paste was added, and they were then examined to see if the necrotic portions of the lobules became blue. No reaction for iodin was obtained in this way. Then after merely removing enough of the liver for proper histological examination, the remainder was ground in a meat grinder and treated with sulphuric acid of about M/5 strength, and a little sodium nitrite. The fluid was then poured off and treated with starch paste. No reaction occurred. The anatomical changes noted in the dog corresponded in every way to those so characteristic of chloroform poisoning. There was a number of ecchymoses on the parietal peritoneum and pleura. The liver was large, very fatty, and slightly yellowish. It contained a small subcapsular hemorrhage on its upper aspect. The kidneys were large and swollen, and the site of marked cloudy swelling. Microscopically the changes again were identical with those which follow chloroform. The liver contained areas of central necrosis involving about one-fourth of the lobule. There was much fat accumulation in the cells that were not destroyed. The kidneys showed numerous casts; and the tubular epithelium was swollen and granular.

Experiment 6—Guinea pig, weighing 560 gm. Given daily for three days subcutaneous injections of 0.2 gm. iodoform (Merck) in paraffin oil. On the fourth day the guinea pig was killed and examined. The anatomical changes were essentially the same as those described in the preceding experiment, but not developed to quite so great a degree.

Bromoform was found to be much more toxic than chloroform; so it was impossible to administer it for two hours to an animal and have any assurance that it would live for forty-eight hours afterwards, and thus give time for the maximum development of the anatomical lesions. It was given by inhalation. In all, eight animals were used. A typical protocol is given.

Experiment 7—A guinea pig, weighing 672 gm. was placed under a bell jar and anesthetized by dropping bromoform through the opened top. It was kept in a state of deep narcosis for forty-five minutes and then returned to its cage and allowed to eat carrots. It remained lying on its side for nearly an hour after returning to its cage. Two days later it was killed by a blow on the head and examined. There were several small hemorrhages in the lungs. The liver was very fatty; and the kidneys were large and grayish. Microscopically the picture in the liver could not

be distinguished from that of a case of chloroform poisoning. Around the central veins were small areas of necrotic cells without nuclei, constituting perhaps one-sixth or one-seventh of the lobule. There was a large amount of fat accumulation. Everywhere the changes were most conspicuous in the central portions of the lobules.

LIVER NECROSIS, AS AN EFFECT COMMON TO ALIPHATIC ALKYL HALIDES.

The readiness with which central liver necrosis, fatty changes, hemorrhages, and edema, could be produced by methyl halogen compounds other than chloroform, immediately suggested the probability that ethyl and ethylene halides would react in the same way. Support for this idea was furnished also by the fact that these substances, like the methyl compounds, readily yield halogen acids outside the body. Niederist[25] has shown that at 100° C. ethyl iodid and water after fifteen hours yielded 98 per cent. of calculated hydriodic acid, and that ethyl bromid after eighteen hours gave 94 per cent. of calculated hydrobromic acid. Ethylene bromid after heating with water for fifty-two hours at 140° to hydrobromic acid.

$$\begin{array}{l} CH_2Br \\ | \\ CH_2Br \end{array} + \begin{array}{l} H_2O \\ \\ H_2O \end{array} = \begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array} + 2HBr$$

Butlerow[26] had previously found that, after heating ethyl chlorid to 100° C. in a sealed tube for ninety-two hours, much hydrochloric acid and alcohol were present.

The following halogen substitution products of ethane have been tried in this work: ethyl bromid, ethyl iodid, and ethylene bromid. Not only do all these substances produce morphological changes indistinguishable from those following chloroform, but also it is possible to obtain evidence that the respective halogen acid is liberated in each case. This evidence is found in the fact that the neutral salts of the respective halogen acids have been found in the urine after the administration of ethyl bromid and iodid. That an acid effect is again concerned is shown by the fact that when sections of the liver are treated with neutral red, according to the method already given, the necrotic portions show a high hydrogen ion content. Although apparently no measurements have been made of neutral chlorides in the urine after the administration of ethyl chlorid, an increase might nevertheless be expected by analogy with the findings after the use of ethyl bromid and iodid. Dreser[27] found inorganic bromin in the urine, both of man and experimental animals, after inhalations of ethyl bromid. Inorganic iodin has been found in the liver of a guinea pig after the use of ethyl iodid by Loeb.[28] The essential morphological changes under discussion in this article have been observed by previous workers to follow the use of ethyl chlorid and ethyl bromid. These have been rather extensively studied by Haslebacher,[29] who also found that the urine became strongly acid and then contained large amounts of casts and albumen, an observation which, in the case of ethyl bromid, had previously been made by Regli.[30]

In our experiments it was found that when given by inhalation the relative power of producing the morphological changes as well as the general toxicity of these substances was greatest in the case of iodid and least with the chlorid. The most toxic of all was ethylene bromid. This was so toxic that a narcosis of fifteen minutes' duration or longer was invariably followed within forty-eight hours by death. In each instance Kahlbaum's preparations were used. Typical protocols follow:

Ethyl Bromid—Adult guinea pig given ethyl bromid by inhalation for eighty minutes. Found dead about thirty hours after the administration. At autopsy the liver was fatty, and microscopically contained definite areas of central necrosis. There were extensive hemorrhages in the lungs. The kidneys were swollen and pale.

Ethyl Iodid—Experiment performed as above, except that inhalation of ethyl iodid was continued for only forty-five minutes. The guinea pig was found dead twenty hours later. The liver was fatty, and microscopically there were areas of beginning central lobular necrosis. The kidneys were pale and apparently edematous. There were large hemorrhages in the lungs.

Ethyl Chlorid—After an inhalation of ethyl chlorid for two hours, the guinea pig was killed two days later. It showed a moderately fatty liver with beginning central necrosis evident microscopically. There were no large hemorrhages in the lungs, and the kidneys were less pale and swollen.

Ethylene Bromid—An adult guinea pig was given ethylene bromid by inhalation for twenty minutes. It was found dead forty hours later. Autopsy showed 2 or 3 cc. of a slightly blood stained fluid in the abdominal cavity. The liver was large and very fatty and showed beginning central necrosis. The kidneys were large and pale and the lungs had several large hemorrhages.

LESIONS PRODUCED BY CHLORAL HYDRATE ARE RELATIVELY INSIGNIFICENT.

If the general theory is correct that the severe morphological changes induced by chloroform are due largely to hydrochloric acid liberated by its chemical dissociation in the tissues rather than merely to the fact that it contains three chlorin atoms, then we should expect that another narcotic substance, which would not yield hydrochloric acid in the body although it contained the same number of chlorin atoms, would not produce these changes. Chloral hydrate is a suitable substance with which to investigate this point because it is eliminated almost completely as urochloralic (trichlorethylglucuronic) acid and therefore is not capable of yielding appreciable amounts of hydrochloric acid. Only a very small portion of it is decomposed, with a resulting increase in urinary chlorides.[31] Experiments showed that guinea pigs, which had been profoundly narcotized with chloral hydrate for from fifteen to twenty hours, failed to show any liver necrosis, hemorrhages, or extensive edema. Only a very slight accumulation of fat occurred in the liver. This was demonstrable usually only by microscopic examination of sections stained for fat. Whipple[32] has stated that he also failed to produce liver necrosis with this agent.

These results seem to afford striking confirmation of the idea that the essential factor in the production of these severe lesions by alkyl halides is the halogen acid formed by decomposition rather than merely the halogen content of the molecule. A representative protocol follows:

Dec. 19. Three adult guinea pigs were used: A, weighing 615 gm.; B, 665 gm.; and C, 485 gm. At 12.30 each was given subcutaneously 0.2 gm. of chloral hydrate dissolved in 2 cc. of water. Fifteen minutes later Guinea Pigs A and B were lying on their sides, but still responsive to stimulation. At 3.00 p. m. there had still been no deep narcosis. Each guinea pig therefore was given 0.3 gm. At 4.30 each was given another injection of 0.1 gm. At 4.45 all three guinea pigs were in deep narcosis.

Dec. 20, 11.30 a. m. Each guinea pig was injected with 0.4 gm. An hour later all were in deep narcosis and were still so at 4.30 p. m.

Dec. 21. Guinea Pig B was found dead in the morning. Autopsy showed reddish purple liver with no appreciable fat accumulation and no noteworthy changes elsewhere. Microscopically there was found no appreciable accumulation of fat in the liver, no necrosis, no marked changes in any of the viscera. At 11.30 a. m. Guinea Pigs A and C were given 0.5 gm. of chloral hydrate as before: At noon both animals were in deep narcosis. At 9.00 p. m. C died; A was still in profound narcosis. Autopsy on C showed slight fatty liver, but no hemorrhages or marked edema anywhere. Microscopically there was no necrosis in the liver.

Dec. 22. Guinea Pig A was found dead at 7.00 a. m. Aside from moderate postmortem decomposition there was no striking changes. Sections of the liver showed no central necrosis.

GENERAL DISCUSSION.

It is a striking fact that certain narcotic agents readily induce marked morphological changes, the most conspicuous of which are central necrosis of the liver lobules, fat infiltration, and a tendency to hemorrhage and edema. This property is particularly evident in those agents whose chemical structure places them in the group of alkyl halides. That this property is not necessarily connected with their ability to induce narcosis is shown by the fact that other narcotic agents (*e. g.*, ether and chloral hydrate), which do not belong to this general chemical group, fail to induce tissue changes which are at all commensurate with those following the administration of the alkyl halides. Moreover, that the mere presence of halogen atoms in the molecule is not the responsible factor is demonstrated by the fact that chloral hydrate ($CCl_3—CH<^{OH}_{OH}$), which, like chloroform ($CHCl_3$), possess three chlorin atoms, produces relatively insignificant morphological effects. Some other factor must therefore be responsible. Evidence has been submitted to show that an important factor is probably the halogen acid (hydrochloric, hydrobromic, or hydriodic acid) which is formed by chemical dissociation of the alkyl halides within the body. That these substances form their respective halogen acids in the body is shown by the occurrence in large quantity of the neutral salts of these acids in the urine. In this respect they differ from chloral hydrate, which is excreted mainly as urochloralic acid, and of which therefore only a small portion is decomposed to give neutral chlorides.

The idea of placing the chief responsibility for these severe tissue effects upon the halogen acids formed in the tissues is based upon a number of experimental findings. Pictures practically identical with that of late chloro-

form poisoning have been produced simply by the administration of hydrochloric acid in suitable concentrations, the only essential difference being that with the injection of the acid the liver necrosis was peripheral rather than central. That these substances form their respective halogen acids within the body is shown by the appearance of their neutral salts in the urine. Alkali, in suitable concentration and combined with hypertonic saline, prevented the liver necrosis and greatly inhibited the other tissue changes. In the series CH_2Cl_2, $CHCl_3$, and CCl_4, the tetrachlorid was the most powerful and the bichlorid the least, in their ability to induce the morphological changes. This comparison parallels the respective amounts of hydrochlorid acid which these substances can yield in their breakdown outside the body; that is, CCl_4 can give four molecules of HCl; $CHCl_3$, three, and CH_2Cl_2, two. Of the ethyl compounds, the iodid was most toxic, the bromid less, and the chlorid least of all. This relationship agrees with their relative chemical reactivities outside the body. The question of how the acid is formed will not be discussed extensively in this paper. Nef,[33] who has extensively investigated the nature of the chemical reactions of the alkyl halides, has submitted a large amount of evidence to show that the halogen acid is dissociated off, leaving a methylene or bivalent carbon residue. In the case of chloroform the type of dissociation, according to him, is:

$$CHCl_3 = CCl_2 + HCl;$$
$$\wedge$$

and in the case of ethyl chlorid it is:

$$C_2H_5Cl = CH_3CH + HCl.$$
$$\wedge$$

He has likewise produced evidence to show that in general the iodides are more dissociated than the bromides, and these in turn more than the chlorides. Our finding, therefore, that ethyl iodid produces the tissue changes more readily than the bromid and this in turn more readily than the chlorid, conforms to Nef's idea of the readiness with which these substances can form respectively hydriodic, hydrobromic, and hydrochloric acids. The applicability of Nef's conceptions of dissociation and dynamic chemical equilibrium to problems of intermediate metabolism has already been under study for a number of years in this laboratory by Woodyatt, with particuliar reference to the chemical phenomena of diabetes.[34]

The tendency to ascribe the anatomical changes of chloroform to the production of phosgene ($COCl_2$), as has been done by Muller,[35] is probably an inadequate explanation, since this substance would almost certainly be quickly hydrolyzed to 2HCl and CO_2 in the body, and again we should be dealing with HCl as an important factor. Binz[36] has considered the liberation of the halogen itself (as molecular halogen) to be the chief toxic factor in all these drugs. There is, however, but little evidence in favor of such a conception; for at least outside the body most of the facts, as Nef has shown, point to a dissociation of a type to yield halogen acid instead of molecular halogen. Our experiments tend to show the existence of a similar type of dissociation within the body.

Fischler[37] has sought an explanation for the chloroform changes in an associated fat necrosis from injury to the pancreas which he noted in a number of dogs. This idea was based on the fact that central necrosis was produced in Eck fistula dogs without the use of chloroform but after intraperitoneal injections of trypsin and hydrazin sulphate, and after severe crushing of the pancreas. He considers some albumen-splitting substance, whose nature he does not discuss, as the responsible factor. Obviously such a suggestion does not explain the production of the changes. It is not surprising that such drastic measures resulted in severe morphological changes, of which one was central necrosis of the liver. It is interesting, however, that degenerative changes most conspicuous in the central part of the lobule (including even well marked necrosis), sometimes followed simply the establishment of the Eck fistula without other experimental procedures. In one experiment, in which he also ligated the hepatic artery, the central necrosis was marked.

Wells[38] has expressed the view that the changes in late chloroform poisoning arise because, although the oxidizing enzymes are suppressed, the autolytic enzymes are left free to digest the cell. There is no reasonable doubt that oxidations, as well as many other metabolic activities, are altered by chloroform, and these other substances under discussion. It is

likewise true that in many respects there is a similarity between the production of chloroform liver necrosis and the self-disintegration of tissue *in vitro* which is called autolysis. But the difficulty in such an interpretation lies in an inability to gain a definite conception of the nature of an autolytic enzyme and to distinguish its effects from those of acids formed in the tissues.

Particular care has been exercised all through this article to state that the halogen acids are suggested to be important factors rather than the only factors involved. Other acids must play a part; and possibly even other substances than acids are concerned. Since chloroform, like other narcotic agents, induces a severe tissue asphyxia, we are compelled to assume the presence of various organic acids, notably lactic acid; and lactic acid, as has been already shown by Fischer and others, is capable of producing extensive tissue alterations. The comparatively slight tissue changes which follow the use of ether and choral hydrate, for reasons already stated, cannot be due to the liberation of a halogen acid in the tissues; but they may perhaps be attributable chiefly to the tissue asphyxia and resultant weak acid formation which they induce. Nor can a halogen acid be a responsible factor in poisoning with phosphorus, which produces morphological changes similar to those of chloroform, except that in the liver the most extensive alterations are at the periphery instead of the centere of the lobule. The mechanism involved here is not clear. Cell asphyxia, however, without doubt occurs; and it is well known that lactic acid is formed in relatively large amounts,[39] which in itself could play an important part. In addition, the possibility should be considered of the formation in the tissue and action of some of the phosphoric acids which are known to occur so easily in the oxidation of phosphorus *in vitro*. As yet there is no direct evidence to support this view. Doubtless also other factors are more or less involved which concern physical alterations in the cell induced directly by the action of the phosphorus.

No detailed discussion will be taken up here concerning the question of whether these morphological changes (necrosis, fat infiltration, hemorrhages, and edema) are to be regarded as primarily acid effects or primarily asphyxial effects. It is of great interest that they can be readily obtained merely by the administration of such an acid as hydrochloric acid. But it is equally true that the administration of an acid also leads to the production of asphyxia. We are, therefore, confronted by the facts that acids give rise to asphyxia, and asphyxia in turn gives rise to acid production. It cannot be assumed that the changes are exclusively acid effects.

In this connection the location of the necrosis in the central part of the lobule is of interest; for this is the region which is farthest removed from the oxygen supply and from compensatory influences carried in by the blood. It is, therefore, the part where, in general asphyxial conditions, asphyxial acids (lactic) would be formed in largest quantity. This is strikingly borne out in Fischler's experiments which showed that interference with blood supply, by ligation of the hepatic artery and production of Eck fistula, was followed by degenerative changes which were always most marked in the centers of the lobules. In the case of chloroform poisoning we might suppose that the central location of the necrosis is due to the fact that in that region we have the greatest total acid formed (asphyxial acids in addition to hydrochloric acid). It is also farther removed from the neutralizing effect of alkalis brought in by the blood than is the periphery of the lobule.

In a previous article[40] it has been shown that newly born pups, which are relatively immune to the production of late chloroform poisoning, owe their resistance to their rich supply of glycogen. The nature of this protective action of glycogen is not clear. It is possible that the observation of Bechhold and Ziegler,[41] that glucose retards the diffusion of sodium chlorid and some other substances in protein gels, bears on this phenomenon. In some work, as yet unpublished, we have observed that the presence of glucose in gelatin and agar gels markedly retards the diffusion of hydrochloric and other acids through them. Fischer and Sykes[42] have recently shown that glucose and other sugars inhibit the swelling of a colloid, like fibrin, in water.

SUMMARY.

The central lobular necrosis in the liver, which has been regarded by some writers as characteristic of late chloroform poisoning, has been produced experimentally with a number of other drugs. It is, therefore, in no sense peculiar to chloroform poisoning. Substances which have been shown to produce a morphological picture indistinguishable from that of late chloroform poisoning are: (a) dichlor- and tetrachlormethane, (b) tribrom- and triiodomethane, (c) monochlor-, monobrom-, and monoiodoethane, also the dibromethane; that is, in general, the halogen substituted aliphatic hydrocarbons containing one or two carbon atoms. Presumably similar results might be obtained with the higher members of the same series.

The mechanism by which chloroform produces its characteristic tissue changes must accordingly be considered as a group reaction. Outside the body the similarities between the chemical behavior of different members of this group have been correlated by Nef on the basis of the type of dissociation which these substances undergo and the differences in their behavior on the basis of the differences to the degree to which such dissociations occur. According to the work of Nef, the group of substances under discussion has the property of dissociating to yield a halogen acid and an unsaturated alkylidene rest. Thus with chloroform the type of dissociation may be expressed thus:

$$CHCl_3 = CCl_2 + HCl.$$

In this paper the view is developed that the changes characteristic of late poisonings with the above named group, namely edema, multiple hemorrhages, fat infiltration, and necrosis are ascribable (1) to acids and (2) to the fact that the amount of acid formed parallels the chemical dissociability of the drug outside of the body.

Favoring the view that acid is responsible for the changes are the following observations.

(1) All the characteristic features of late chloroform poisoning have been produced merely by the administration of hydrochloric acid, except, however, for a different distribution of the liver necrosis.

(2) The arears of central necrosis produced in the liver by the various substances under discussion give an acid reaction to neutral red.

(3) Sodium carbonate in a hypertonic sodium chlorid solution markedly inhibits the production of the lesions.

In favor of the view that the respective halogen acids play an important part are the following.

(1) After the administration of some of these drugs there has been noted an increase of the neutral salts of the halogen acids in the urine, a fact which indicates that the corresponding halogen acids must have been formed somewhere in the body.

(2) The necrosis-producing powers of dichlormethane, chloroform, and tetrachlormethane parallel the amounts of hydrochloric acid which these substances theoretically can yield in their breakdown outside of the body. Likewise, the power to produce tissue changes exhibited by the ethyl compounds varies directly with the ease with which they form their respective halogen acids *in vitro*.

(3) Ether and chloral hydrate which do not yield halogen acid in their breakdown in the body likewise also do not produce necrosis. They induce only edema and fat infiltration to a less marked degree.

The suggestion is made that the halogen acid (hydrochloric, hydrobromic, or hydriodic acid), directly liberated in the process of dissociation, may be the important factor which makes the tissue changes seen in poisoning with chloroform and other alkyl halides so different from those following the administration of narcotic drugs of a different type.

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SOME PSYCHIC FACTORS OF SURGICAL ANESTHESIA . FIELD OF CONSCIOUSNESS AND FOCUS OF ATTENTION . APPREHENSION AND APPRECIATION . ESTABLISHING CONFIDENCE . PRECONCEIVED OBSESSIONS . TACTUAL, PHYSICO-CHEMICAL AND ESTHETIC SENSIBILITY . OIL OF ORANGE . MORPHIN . CONTROL DURING INDUCTION . SENSATIONS OF FEAR AND HELPLESSNESS . GRADUAL INDUCTION.

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IT IS ONLY RECENTLY that any attempt has been made in the United States to confer upon the administration of anesthetics the dignity of a specialty. The devotion by a medical man of his whole time to the study and administration of anesthetics was rare in this country until a few years ago, although in Great Britain and in Canada the professional anesthetist has been recognized for a long time. This, together with the demanding by certain states that a graduate in medicine must spend a year in a hospital in which instruction in anesthesia is given by a visiting anesthetist, before he can be granted an examination for license to practice; the numerous articles on anesthesia which now appear in medical journals; the formation of societies of anesthetists; the publication of the Anesthesia Supplement of the AMERICAN JOURNAL OF SURGERY, and this YEAR BOOK; all these and other circumstances indicate a scientific interest in anesthetic matters hitherto unknown among us. It must be borne in mind, however, that, in spite of all this the field is new. Much that is written or done is erratic, but such is only the necessary wandering in a region unexplored and therefore little known.

It is a matter of time and of earnest, conscientious effort to open up and cultivate this new field of surgery and make it yield its quota toward successful operative procedures. And so as an effort in this direction let me ask your attention at this time to *Some Psychic Factors of Surgical Anesthesia.*

First, however, let me say that I do not refer to direct hypnotic influence. It is true that a patient will be calmer and more submissive in the presence of one personality than in that of another. In the broad sense such a condition is indeed hypnotic in its nature, since hypnotism depends for its effect upon the willingness of one personality to suspend its own activity and follow the suggestions of another and the hypnotic state is only the realization of this passivity. Such a simple condition, however, as that of which I shall treat, is so common in everyday life, so within the power of everyone, that to dignify it by calling it hypnotism would be misleading.

The symptoms of hypnotism, in its strict psychological sense, can be made to appear in about eighty per cent. of people as they come and go. This means, however, that in these people phenomena can be induced which the psychologist can recognize as hypnotic. To a layman, even to the subject himself, these phenomena usually mean nothing. For producing hypnotic phenomena which will be appreciated by the laity, the number of persons available is comparatively small. A selection of subjects must be made and a certain amount of training is necessary. Further, the complete hypnotic state which can be made to involve analgesia is possible in only a still more restricted number and for actual use in surgery would require on the part of the patient intelligence, long training and consequently a patho-

logical condition for which the operation could be postponed indefinitely.

The power which the anesthetist is called upon to exercise belongs to hypnotism only as any phenomenon in every-day life, which involves influence, belongs to hypnotism. Such is the influence the successful salesman exercises over his customers; the orator over his audience; the looker-in at the shop window over others who stop and look because he looks; of the crowd moving in a particular direction which by its movement causes you to join it. These phenomena are indeed hypnotic, but to refer to them as such in practical life would create wrong impressions. So with the dealings of the anesthetist with his patient. I shall treat of them without alluding to hypnotism.

Now in order to make my paper clear let me dwell for a while upon its terminology. Throughout I shall consider the patient's mind as it actually is when presented to the anesthetist, and in all instances all that the anesthetist has to do is to deal with it as it is. He will fail if he attempts to manage it from a theoretical standpoint and make it what it cannot be. There is one factor of great value to the anesthetist. It is that, so far as it is concerned with anesthesia, the content of the various minds that come before him does not vary much in quality. The intensity of the ideas in them may differ but as a rule the quality does not. In order to comprehend this content let us consider briefly the normal mind.

We all feel that we have present in our mind a large number of ideas. Of these we say we are conscious. As I pen this paper I am conscious of my writing materials, of the table on which I am writing, of an electric lamp before me, of some ethyl chlorid and chloroform on the table, of some of the walls of the room, of the noise of gongs on electric cars outside my room and of several other things besides the fact that I am writing. Of these I say I am conscious and I call this group of ideas *the field of consciousness*. Whether all the ideas present are equally clear and distinct is another matter. What it is essential to recognize first is that I am possessed of a field of consciousness which may be more or less extensive or limited and that this field of consciousness is coextensive with and another name for the totality of ideas of which, at any one moment. I am more or less clearly conscious.

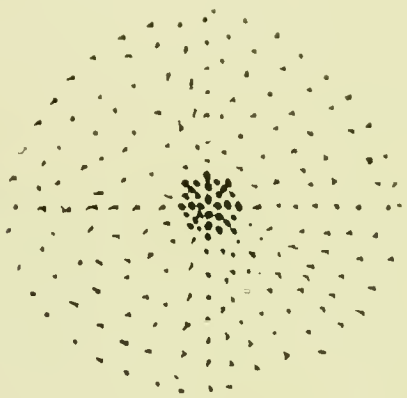
I notice, however, not only that there is a marked difference in the clearness and distinctness of the different parts of this field of consciousness, but that one part stands out preëminently distinct above the rest. The subject on which I am writing and my effort to reduce it to visible form especially occupy my mind. This forms a sort of center or focus of my mind. Therefore in the field of consciousness, this special point on which the mind is concentrated I call the *center* or *focus of attention*.

Further, there are continually coming into my mind ideas of which I was not previously conscious and which have no immediate connection with my present environment. They are not due directly to sense impressions. The hissing of a locomotive outside my hotel, an idea which has entered consciousness through an auditory sensation, suggests a locomotive with its train of cars stopping at the station near my house which is several hundreds of miles distant, an idea of which I was not previously conscious. This in turn awakens the idea of the killing of a man by a train at this same station and to whom I was called after the accident. Now the closing of the gates of the elevator in the hall produces not only an auditory sensation but also reminds me of the eagerness with which I awaited the arrival of a friend, also with an accompanying chain of ideas, none of which ideas is immediately connected with my present environment. Now whence did these ideas come? Not directly from sense impression but indirectly. They were present in my mind but were not in consciousness. Some special activity called them forth from somewhere else. This region in which all such ideas are I call the *region of the subconscious* or simply *subconsciousness* and the boundary line between it and the field of consciousness I call *the threshold of consciousness*.

If now I represent diagrammatically the field of consciousness by dots arranged in a certain way, the indefinitely extended blank space all around it will be the region of subconsciousness, some of the contents of which, by the presence of the proper stimulus, will

come over the threshold and become a part of consciousness.

We note then that there is a field of consciousness which may receive new elements from a realm of ideas of which we are not conscious known as the region of subconsciousness, and when such an idea passes over the threshold into consciousness I say I *apprehend*



it. If now that idea becomes the object of attention, or if any other idea assumes such special importance I say I *apperceive* it or it is *apperceived*. By *apprehension* then I mean the entrance of a psychical state into the field of consciousness; and by *appreciation* I mean the stationing of a psychical state at the focus of attention, indicated in my diagram at the center of the field of consciousness by a group of dots closely placed, six on any one diameter. The number of ideas that may constitute the focus of attention I call the field of apperception or the scope of attention. Since Leibnitz, Kant and other philosophers and psychologists have used these expressions in different senses, it has been not only not useless but absolutely essential for me to make known exactly what these terms signify in this paper, if ambiguity is to be avoided.

Let me now consider in detail the psychic phenomena of patients for anesthesia and which the successful anesthetist must have clearly before him. There are several ways along which I might lead you in doing this. I could begin with the simpler psychical phenomena and proceed to the more complex. This might be the best way were I writing for psychologists whose interest in the subject is purely from the standpoint of psychology. But as it is my privilege to appeal to medical men whose interest is clinical I shall consider the phenomena as they occur chronologically before and during the anesthesia and while discussing these phenomena I shall lay down the rules for controlling them.

But let me say right here, once for all, that except under certain special circumstances, which I shall explain fully, I do not believe in controlling the mind of the patient by drugs. It is always best to guide or subdue psychic phenomena by psychical technic.

The first mental perturbation of importance in anesthesia is that due to the disturbing ideas implanted in the patient's mind by friends or visitors. They seem to delight in making it appear to the patient that they have experienced exactly what is before him and they call his attention to all the real or imaginary concomitants that they experienced in connection with their anesthesia. Thus, in the mind of the patient, who, under the circumstances, is peculiarly receptive of such information, ideas are implanted which cause him to anticipate his coming anesthesia with dread or even with fear. Even if he tries to dismiss them from his mind and succeeds in banishing them from consciousness they remain in subconsciousness to appear during the induction and cause disturbance if they are not held in check by the anesthetist.

Such ideas must be overbalanced by those that are correct and assuring. Success in doing this depends entirely on the *manner* in which it is done. If the anesthetist go directly to the patient and tell him that his friends are mistaken and explain the fact he will fail almost every time. Patients do not believe all that their nurse, surgeon or anesthetist tells them. They may have perfect confidence in them, but one element in this confidence, paradoxical as it may seem, is a belief that it is the duty of the medical attendant to conceal all detrimental information and to make only assuring statements.

In dealing with such a case then, the endeavor of the anesthetist should be to have his patient believe that he knows his business and that he has perfect confidence in his patient taking the ether well. The method should be by action not words. An illustration will make this clear.

Illustrative Case.—Mrs. Smith is in bed in a ward awaiting operation tomorrow. Her mind is anxious because of the discomforting stories told her about the anesthesia. I go to the ward with the sole purpose of removing Mrs. Smith's fears. As I enter I apparently do not notice Mrs. Smith but go to Mrs. Jones' bed, which can be clearly seen by Mrs. Smith and I examine Mrs. Jones in whom I have no interest, taking care that Mrs. Smith sees me. I start as if to leave the ward and as I pass Mrs. Smith's bed I turn apparently in surprise to see her there and then go and converse with her on any subject except the anesthesia. I leave without mentioning it. When, however, I am about to leave the ward I return to Mrs. Smith and say: *"Mrs. Smith I think I'll tell you that while we were conversing I looked you over and tomorrow you are going to take the anesthetic well."* The train of reasoning I thus set up in her mind is this: That doctor is going to give me the anesthetic tomorrow. My friends tell me it is disagreeable and dangerous. If it were so and were I going to do badly under it, doctor would have said nothing to me about it. Since, however, when he was not obliged to tell me about it, indeed did not know I was here, he came back and told me I would be all right, I think I will be, for he knows more about it than my friends do." Thus all the detrimental ideas have been removed and assuring ones substituted.

A second source of mental disturbance is the waiting by the patient for the anesthesia after he has been told the anesthetist is ready, or has been removed from his room for it. During this time all sorts of ideas form in his mind and, however false or grotesque they may be, their continuance may so augment their intensity that they may assume the importance of verities and play the part of impressions formed by the senses.

During such a period of waiting the mind is peculiarly receptive of impressions by the senses, particularly those of sight and hearing. For the patient, this interval of waiting is a period of dread, even of terror and fear, and impressions made under such circumstances are deep and lasting. Even if the sensory stimuli be weak, they leave their impression in subconsciousness and under favorable circumstances a revival of these ideas is possible. It should be remembered by the anesthetist that the persistency of an idea in subconsciousness, the ease with which it can be brought over the threshold of consciousness, the intensity of this idea when it is apprehended, as well as its vividness when apperceived, depend not only upon associated ideas, but also on the condition of the mind when the first impression was made, and the clearness and distinctness of the integral parts of the field of apperception at the time the idea is apprehended. It is necessary only to question a person years after he has taken an anesthetic to know how accurately and vividly he can recall circumstances, particularly unpleasant ones, that attended the induction or accrued while he was waiting for the anesthetic. In many cases such impressions remain as only unpleasant remembrances, in others the disturbance is so great as to be of pathological importance. It must be remembered that such patients seldom are seen afterwards by the surgeon or the anesthetist but the psychiatrist knows them well. At times a subconscious idea, implanted while waiting for an anesthesia, assumes the importance of an obsession and this may manifest itself only years after the anesthesia. Let me cite an instance:

Illustrated Case—A. B.: Male, 32 years old, liquor dealer, of robust health, mild drinker, presented himself to a psychiatrist on account of certain obsessions. They were three in number. First, a fear of going to a doctor's office. Second, fear of any sharp instrument, particularly of a knife; a fear that he might be killed by it or an idea that he must kill someone with it. Third, a fear of death. He said, *"I can't reason myself out of it."* These obsessions were traced back unmistakably to conditions connected with a waiting for the anesthesia at two operations. The first, fourteen years previous for appendicitis. The patient was told the diagnosis and what would have to be done, but in order to obtain the consent of his parents he was kept waiting in the operating room for two hours, which were to him as he expressed it *"a period of great suspense and dread."* The second operation, for hernia, was ten years later, that is, four years previous to his application for treatment for his obsessions. His record shows that he was rushed to a hospital sixty miles distant, taken to the operating room and was kept on the operating table for some time before the anesthesia was started. The patient says, *"knives were all around me. I lay there in fear of death all this time. The anesthetic didn't bother me, but I feared death and now when any fear or anxiety overwhelms me, I see imaginary knives and fear knives, so that even the sight of a sharp instrument makes me fear myself."*

This is a very fair example of the late appearance over the threshold of consciousness of ideas stored away in subconsciousness by the improper care of a patient awaiting anesthesia. The circumstances of terror and fear, in the midst of hospital surroundings which were such as they should not have been, made possible impressions in subconsciousness which entered consciousness and occupied the focus of attention the moment that any fear or anxiety let down the barriers of the region of the subconscious and permitted them to be apprehended and apperceived.

There is only one way to prevent such a

mental condition. It is to keep from the senses of the patient to be anesthetized anything and everything that can disturb him or impress upon him undesirable ideas. He should not be removed from his bed or otherwise disturbed in his regular living until the anesthetist is actually ready for him. He should not be made to lie on a stretcher or on an operating table waiting a delayed anesthesia. In the anesthetizing room there should be no instrument or anything else to suggest operative work. All should be quiet, no slamming of doors, no passing to and fro in the room, no whispering, no talking of operations, and anesthesias, or other hospital matters. Everything even to the most trivial circumstances, should make for tranquility of mind, and the leaving of pleasing impressions on the sensorium of the patient. I shall have to recur to this when I speak of the induction of anesthesia.

A third disturbing psychic factor in anesthesia is a lack of confidence in the anesthetist by the patient. If perfect trust is wanting the patient will try to control the induction, thereby disturbing it, particularly when co-ordination of the senses is wanting. This negative condition, or lack of confidence, becomes positive distrust if anything that may be interpreted as deception occurs, and early in the induction the patient antagonizes the anesthetist. To prevent distrust and establish confidence, care must be taken to tell the patient the truth about the anesthetic and this *at the proper time.*

First. The patient should not be told that he will not mind the anesthetic and that he will go right to sleep, for if he is told so there will be trouble. The odor of anesthetics is disagreeable to most people. If the patient has been told he will not mind it, when he inhales it and doesn't like it, he feels he has been deceived. Again he does not go *right to sleep*, as he has been told he would, at least as he interprets *going right to sleep.* The phenomena of time is variable. The estimate of the spacing of its components and, therefore of its length is not absolute. However many seconds a pendulum may tick, the estimate of time is not made for the individual by a chronograph. Succession, as a cerebral phenomenon, determines it for him and his estimate differs from that by some arbitrary standard, as that of a clock, for instance, according to the action of the brain or the condition of the patient's mind. Certain drugs greatly modify it. Cannabis Indica lengthens it; pleasurable states shorten it; pain, anxiety, fear, prolong it. The patient, who is being anesthetized, and who dreads the anesthesia, thinks it a long time before he goes to sleep and if he has not been informed rightly, a disturbing cerebration results. He reasons thus: *"I was told that I would not mind the ether, but I do; I was told that I would go right to sleep, but I dont;"* and he continues, *"so the surgeon said the operation would not hurt me, but now I think it will,"* and consequently the patient becomes restless. This train of reasoning reacts upon itself, calls up or creates other disturbing ideas that in their turn set up new cerebral functionings, all of which prolong and disturb the induction and unless the patient be kept profoundly asleep, even will embarrass the anesthesia by the intermittent play of subconscious ideas.

There is only one way for the anesthetist to proceed. Let nothing be said to the patient about the anesthesia before he enters the anesthetizing room. There let all be frankness. The anesthetist now should approach the patient in a quiet, assuring, but matter of fact way, and avoid giving the patient any impression that he is trying to soothe him into submission. Let him ask him, for instance, if he ever took ether before? If he answers *"yes"* ask him if he liked it? To this question the replies may be various. Some will say, *"No, I didn't, it was fierce."* Others, *"No, but I had to take it and so I made the best of it."* Some may say, *"I didn't mind it much."*

Or to the first question the answer may be negative. However, whether the reply be *"Yes"* or *"No,"* let the anesthetist say to the patient, *"Well, now, listen, I have something to tell you, people who take an anesthetic don't like it. They don't like the smell of it and you won't. You may find it very unpleasant but if you will breathe regularly and deeply, then what is disagreeable will go away more quickly than it will if you do not breathe well."* This simple, plain, frank statement will accomplish two things, it will establish in the patient directly a confidence in the anesthetist and directly a confidence in the surgeon. When the pa-

tient finds the odor of the anesthetic unpleasant, he realizes that the truth has been told him about it and he believes that since he has not been deceived in respect to what is disagreeable about the anesthetic, also he has not been deceived about the rest of what is to be done.

Again frankness will secure the assistance of the patient at a time when it is needed. He feels that the anesthetist has put upon him the responsibility of doing away with what is disagreeable. It is not by removal of the mask or by anything else that the anesthetist may do, but by his breathing regularly and deeply that the unpleasant part of the anesthesia may be shortened. And after he has taken a few deep breaths he doesn't care whether he breathes ether or perfume.

A word should be said about the use of oil of orange in connection with the induction of anesthesia by ether. There are three elements that combine to make disagreeable the inhalation of ether vapor. The first is the touch of the vapor with the faucial membranes. This unpleasant sensation may arise from the touch of any gas, even an inert one. I call this *the tactual element*. The second is the direct irritation of the mucous membrane by the ether vapor. I call this *the physico-chemical element*. The third is esthetic in character. It is merely a question of personal like or dislike of the odor of ether vapor. To some persons the odor of ethyl ether is pleasant, to most persons, however, it is unpleasant. For the majority of those who have been put to sleep by it, it is repulsive especially if harsh methods of anesthetizing were used. In many such persons this feeling of dislike is a complex one, due mostly or even wholly to association ideas. The impressions received at a time of anxiety and dread, and a faulty administration, become associated with the persistent odor of the ether and all is fused into a complex feeling of disgust which is called forth whenever any of the original elements, particularly the odor of ether, impress the sensorium. This I call *the esthetic element*. The value of the oil or so-called *essence of bitter orange* is wholly confined to a masking of this odor of ether. It is able to do so if concentrated and used properly, for the odor of the terpeneless oil of orange is considerably stronger than the odor of ether vapor; how much so it is difficult to determine. The sensations of sight, hearing and some others increase in proportion to the logarithm of the stimulus, but the relative increase in the sense of smell cannot be determined so accurately. I myself am unwilling to allow anything of even so large a range as twenty times as strong as the odor of ether for the odor of the oil of orange. The ponderous nature of the odoriferous emanations of oil of orange and the extremely rapid volatility of ether when absolute, together with the rapidity with which ether obtunds the olfactory nerve, must necessarily give too high figures for the oil of orange and too low figures for ethyl ether. There is some difference, however, in favor of the oil of orange.

To use it for masking the odor of ether about two minims of the terpeneless oil of orange or its equivalent of alcoholic extract should be placed in the inhaler near to the nostrils, but not too near, else a preponderance of the odor of the oil will be had and this itself is irritating to some noses. If the proper amount is used and correctly placed in the inhaler, the odor of the ether vapor may be so masked that it will not be repugnant to certain patients. There are those who prefer the odor of the ether to the combined odor.

I have been asked: *"Would I never control the patient's mind by drugs?"* In reply, I say, I wish no morphin preliminary to the anesthesia except in three classes of cases. My reasons are these:

(1) Patients differ so in their idiosyncrasy to morphin that a correct dose is difficult to determine.

(2) It does away with the anesthetist's two most important waymarks. These are the character of the respiration, which varies with the operative procedure, and the light reflexes of the pupils.

(3) Unless administered in undue quantity, morphin prolongs the induction and necessitates more ether to be used, since it diminishes both the number of respirations per minute and the amount of tidal air at each respiration, and, consequently, the amount of ether vapor that can be inhaled within a given time.

(4) Morphin prevents the patient clearing

the larynx if necessary. Should any liquid or solid substance find its way into the larynx during anesthesia, the patient without an opiate can usually be made to cough it up. This is effected by a removal of the anesthetic, allowing a recovery until the vomiting center is reached, then if the patient does not expel it without assistance, tickling the back of the throat and it will be coughed up.

So, especially in adenoid and tonsil cases, if morphin be given preliminary to the anesthesia, trouble may arise not only during the operation, for the reasons just mentioned, but after the patient has been put to bed, blood, oozing from the nose or throat, will find its way into the larynx and trachea because the patient cannot clear the pharynx.

(5) Morphin favors sudden respiratory arrest with a slow, intermittent respiration after it has been restored. This occurs upon sudden stimulation of the solar plexus or hyperstimulation of the sympathetic ganglia which lie on the anterior surface of the sacrum.

(6) Morphin favors postoperative nausea and vomiting.

(7) Morphin may allow asphyxia during recovery. Should the patient vomit and because of the opiate an inability to completely expel it exist, some vomitus may be aspirated into the lungs with serious results.

These are some of my reasons for not using morphin. The second reason I believe to be sufficient in itself.

The three classes of cases in which I demand its use are these:

(1) Nervous cases with marked physical manifestations. In these, the mental disturbance may precede and cause the physical. Such a case would be an accident emergency. The trauma demanding surgical interference may be slight, but the mental shock from circumstances attending the accident may be great and as a consequence the patient has marked respiratory and cardiac disturbances. Or the physical condition may precede and be the cause of the mental disturbance. Such a condition exists in the patient with an ordinary exophthalmic goitre. Many such patients have died while being wheeled from their bed to the anesthetizing room because of the combined fear and nervous bodily state, so I wish such patients to have sufficient morphin before the anesthesia to cause them to go to the anesthetizing room with a tranquil mind.

(2) The second class is that of pronounced alcoholics. The disturbance on the table caused by these patients is not an exciting power of ether, but the peculiar cerebration which dominates the alcoholic whenever he is out of a restraining contact with his environment. We see it manifest as he sits in the car without newspaper or companion, in the restaurant if he is alone at the table, when he is in bed about to go to sleep, as well as when partially under an anesthetic. It is a peculiar exciting cerebration. Opium prevents this brain activity, so I wish the alcoholic to have morphin to reduce him to a normal subject.

(3) The third class is that of young or middle-aged men of a marked athletic type or build. Such, as a rule, secrete a tenacious mucus which forms diaphragms in the smaller tubes of the lungs and prevents an interchange of both ether vapor and air between the lungs and the blood. As a result there is marked cyanosis and the induction is very tedious and difficult. Small doses of atropin will prevent this. But atropin alone, in these cases, will so intensify an already powerful action of the abdominal muscles, and so increase the extent of the excursions of the abdominal walls that should the parieties be involved in the operation, the ease or success of the surgeon's work will be interfered with. Therefore, for these cases I demand a little morphin, not for purposes of anesthesia, but to counteract any hindrances for the surgeon that the atropin may set up. With these three classes of cases my use of morphin begins and ends. I am sorry to have to use it in these, but of two evils I choose the lesser.

Turning now to the patient, as he lies upon the table in the anesthetizing room, it is necessary for the anesthetist to remember that he must deal with the patient's mind as it is. What the anesthetist has to do is to keep below the threshold of consciousness any undesirable elements and to control and guide those that constitute the field of consciousness. He should remember that it is useless to appeal to the patient's will. Frequently the anesthetist explains to the patient what the anesthesia may be like and requests the patient to behave

thus and so. Such is of no use. At the time the appeal to the patient is made he understands and intends to obey, but at the time when the assistance could be of help the patient has no will.

The most highly differentiated cells of the central nervous system are affected first by the anesthetic. Of psychic states, the higher the order the earlier are they disturbed or extinguished. Therefore, we find the will crippled first. Very early in the induction it becomes weak and it continues to get weaker until soon it not only is unable to direct and control the movements of consciousness, but also cannot resist the disturbing play of associations and the inroads of ideas from subconsciousness. These psychic states consequently assume undue importance; associations and ideas, whose power to impress a weakened sensorium increases as the volitional control diminishes. The anesthetist must appreciate this condition. If he does he will not rely on any help from the patient and will gain control of the patient's mind before its wild play has caused trouble. This may be stated a little differently for emphasis, because of its importance. At the time when the patient's assistance is needed apperception is not possible except in a very special and limited way. The patient has practically no power of attention, none except as created by something that someone says or does, for it is possible to call forth by suggestion for a short time an effort on the part of the patient which may be called momentary or transitory apperception. It has the characteristics of attention because the psychic state has a focus more or less sharp, but it is only for a moment. Therefore, in this respect it differs from normal attention or act of apperception. This lack of persistency, except as continuance is maintained by external means, is the important point for the anesthetist to bear in mind.

Therefore, there should be no disturbance present to influence the patient's mind and the necessary control during the induction of anesthesia should be by the anesthetist alone, and it is well for him in assuming this command to know how this realm which, for the time being, he has to govern, differs from a normal mind.

Consciousness is not lost, but disintegrated. The elements of the field of consciousness, as well as those of the field of apperception, no longer work together harmoniously. Unified apprehension and apperception which constitutes the ego what it is do not exist. Therefore, the ego, the personality, is non-existent. Emphasis should be laid on this word *unified*. There is still apprehension and also a sort of apperception during the beginning of the induction of anesthesia, as has been shown. The field of consciousness is narrowed and continues to narrow as the induction proceeds. As the field of consciousness narrows, subconsciousness, which is always responsive to association processes, assumes a more and more important activity and pours its ideas in increasing numbers over the threshold into consciousness which now consists of units uncontrolled by any true apperception and, therefore, are ready to follow any line of association that may be suggested. At this time psychic complications or associations of disparate senses may play not only *an* but *the* important part in the association train. Such associations of disparate senses are more or less common in normal waking existence, but they are commoner during the induction of anesthesia, especially that of chloroform, since then marked hyperesthesia of the senses of hearing and of touch exist. But the difference for the anesthetist to remember is that in waking life they are under control, while during the induction of anesthesia they are not.

A patient at such a time is more like a man in that stage of sleep when dreams are possible, but differs from the dreaming sleeper in that the state of the partially anesthetized patient is more fixed. The complication cannot completely arouse him.

To illustrate what I mean, let us recall some everyday experiences. The sound of an explosion is heard. What caused it is not known, but a weak visual image of flying rocks or of a shattered building and scattered debris accompanies the sound according as the hearer has had some experience with the blasting of rock or a powder mill explosion.

A band is heard in the street. Whether it advertises some circus or precedes soldiers marching is not known, but a weak visual image of a college commencement procession, headed with its band, or the passing of troops is had, according as the one or the other has been an object of marked attention in the past.

We see a violin and are conscious of a weak auditory sensation of its clang. We see some favorite fruit, either natural in a store, or artificial in a mu-

scum, and we say our mouth waters, that is, a momentary sensation of the taste or flavor of that fruit is experienced when it is seen. In these instances the disparate senses of sight and of hearing or of sight and of taste have been associated. So a stimulation of any one sense may arouse associated ideas, not only of that sense but of any other of the senses.

These disparate sensations or complications may be and are usually very weak in ordinary life. It is not, however, their intensity for the waking subject that is of importance to the anesthetist. It is their existence at all, and especially the fact of their necessary existence. If this is borne in mind, the anesthetist will understand not only how psychic complications can and do arise, but he will expect them and anticipate their coming. He will know that in the patient's going to sleep by the anesthetic a disturbance of one sense may arouse a disturbing train of ideas in that or in any other sense, and that not only the sense aroused primarily, but that activated secondarily may in turn set in operation association trains of ideas which, once started, may become itensified almost indefinitely according to the law of cumulative psychic action. In other words, if during the induction of anesthesia association processes are allowed to get to work, inasmuch as coördination is lost, subconsciousness, which assumes an importance inversely as the activity of apperception at the time being may send over into consciousness ideas of such a kind or in such numbers that dissociative activity may generate from them trains of mental experience, the wildest and most exciting of which the human mind is capable. If the patient should translate any of this psychic activity into bodily action, as he could and often does do, a so-called secondary stage will result and the anesthetist will have a fighting patient very difficult to subdue.

On the other hand, if all disturbing influences are kept from the patient, and if by any means apperception is kept directed to one idea, all other apprehended units will disappear and the field of apprehension will become narrowed down and finally limited to the field of apperception. Thus the patient will be kept under control until the anesthetic has eliminated all possibility of sense impressions and also subdued the motor centers.

The anesthetist then should talk to his patient during the induction. Never for a moment should he allow the patient's mind to run its own course, for he cannot tell when some vivid idea may arise and upset an otherwise smooth anesthesia. In talking with the patient he should never ask a question or suggest any unpleasant idea. If a question is asked, the patient may answer, but since coördination is lost very early, the speech center is likely to continue its activity and a coherent reply will pass into incoherent talking and then into an inarticulate jabber, which will continue until the center yields to the anesthetic. This, however, is not likely to be soon, since during the activity of the speech center the patient does not breathe deeply or otherwise well, and consequently the induction is prolonged and disturbed.

What then shall the anesthetist say to the patient? If he analyze the content of the patient's mind he will find the answer to this question. There are two ideas prominent in the mind of every patient who comes up for anesthesia. One is that *something may go wrong;* the other *that he may be cut before he is analgesic.* The first idea is a peculiarly oppressive one. The mind that could bravely encounter danger, were the danger visible, becomes fearful and weak if the danger be hidden and particularly if there is a question whether it does or does not exist. Therefore, the patient who as a rule dreads the anesthesia more than he does the operation is in a distressing state of mind, which is not conducive to a good anesthesia.

In talking to his patient the anesthetist should confine his statements to what the patient needs to know, namely, tell him that *everything is all right.* The same words need not be used constantly, but the phraseology may be varied according to the command the anesthetist has over the language the patient understands. However, even this idea must be expressed in sentences comparable with the patient's scope of attention. While for the normal mind the scope of consciousness varies with the way objects are grouped or the rhythm read into successive sounds, the scope of attention is pretty constant, reaching a maximum in six isolated sensations, as six letters or dots for sight, or six beats or syllables for hearing. Now further, for the patient who is passing under the influence of an anesthetic, the number of isolated elements that can stand

in the focus of attention constantly diminishes until it becomes zero. This means that the anesthetist in talking to his patient at the beginning of the induction should limit his sentence to six syllables clearly enunciated, and as the induction proceeds would shorten his sentences or phrases to five, four, three and two syllables, and end with only one. Such a series would be:

(6) You are do-ing all right.
(5) Every-thing is all right.
(4) You are all right.
(3) All is well.
(2) All fine.
(1) Fine.

It is best to have important parts of several successive sentences identical. This assists the attention of the patient and emphasizes the salient idea.

By thus talking to the patient, the anesthetist not only keeps the patient's mind under control, preventing inroads of ideas from subconsciousness, but he gives the patient the assurance he needs and prevents his fears disturbing the anesthesia.

The anesthetist hardly needs to be reminded that the syllables should be spoken in a somewhat loud tone and be clearly enunciated. It is essential that the patient understand what is said when his mind is confused by the anesthetic. As the scope of apperception diminishes, the field of consciousness disintegrates and the boundary between it and subconsciousness becomes less definite. Subconscious ideas then, are more easily apprehended. The anesthetist will understand that by continually reminding the patient that *everything is all right* he creates for the moment a focus of attention, a field of apperception, which as we have seen is, under the circumstances, practically coextensive with the greatly narrowed field of consciousness. So in thus creating a field of consciousness of such a nature, he for the time being erects a barrier at the threshold of consciousness and excludes subconscious ideas.

Keeping in mind, therefore, this fact of the existence of a continuous series of momentary fields of apperception which continually narrow as the induction proceeds, the anesthetist will understand further why he must lessen the number of syllables in his sentence pronounced to the patient as the induction goes on, and still again why he should take care that emphasis be upon the word representing the salient idea which he wishes to impress on the patient's mind. Hence, at first *everything* and *right* should be emphasized and later *right, fine, well.*

The second dominant idea in the mind of the patient is that he may be cut before he is analgesic. To care for this mental state, negative treatment is the best. This consists in an endeavor not to permit the idea to be converted from an apprehended idea into an apperceived idea, or if it has sunk into subconsciousness, to prevent its being aroused and entering the field of consciousness. To accomplish this, *let the patient absolutely alone during the induction.* Do not touch him or allow him to be touched for any purpose whatever, except some extraordinary occurrence render it imperative. Also he should not be strapped on the table, and no straps or other possible means of restraint should be visible. There should not be any orderly or nurse around whose presence could suggest restraint. The patient should be allowed to assume for himself the position which is most comfortable for him, except, of course, if he desires to go to extremes and get into a side or a prone position. This I have never seen a patient do. The only exception to this concerns the head, which, whether comfortable or not, should always be in a position from the beginning of the induction to allow a free airway.

Again, on account of its importance, let me say that by leaving the patient alone is meant not touching for any purpose. No nurse, clergyman or friend should be allowed to hold or touch his hand. If sheets or other things about the table are not strictly in accord with the hospital regulations, let them be just as they are. If the surgeon is in a hurry, let the patient alone. Do not attempt to save time by getting the patient *into position* until full surgical anesthesia has been induced. To do so will be to lose time. The only exception to this is that the patient may be scrubbed up while the induction is going on, providing it has been begun and is well under way before any of the anesthetic has been administered. In such a case, tell the patient he is to be washed up, and that while the scrubbing is going on you will give him the anesthetic. Then do not begin the administration until the prep-

aration is well under way. Thus the patient when he is partially anesthetized will not misinterpret what the nurse or orderly is doing to him. The scrubbing up will at first be an object of apperception and throughout will remain at least an apprehended idea. Why is this to be done? Because if the patient is touched during the induction, inasmuch as coördination, a regulating contact with environment, is lost, he will interpret a touch of any kind as the beginning of the operation and he will let the anesthetist know that he is still conscious. This he will do by some motion of limbs or head. To his abnormal mental activity, which his surroundings cannot check up, his movements seem small, but as a matter of fact he is thrashing around on the table and restraint may be but is not always necessary. If now he is held he will interpret the restraint as for the operation and the anesthetist will have a fighting patient. Most of the so-called secondary stage is due to the patient trying to let the anesthetist know that he is not ready to be cut.

The patient may not lie perfectly quiet on the table. He may move an arm or a leg as he would were he going to sleep naturally. This is of little consequence and need not receive attention unless a leg falls off the table, when it must be replaced. Very gentle handling must be had, however. If an arm or hand is held up and it is likely to fall on the inhaler or the field of operation, it must be guided to the place where it should lie. To do this the anesthetist or any one else should never take hold of it. Such an attempt will be misinterpreted and give trouble. Let the anesthetist or his assistant place his own hand where the patient's hand will fall on it, and when it has fallen, by a slow, gentle movement guide it to where it should be. The patient distinguishes between the anesthetist touching his hand and he touching the hand of the anesthetist. The former he will misinterpret and respond to; the latter he will understand and will remain passive.

Two more psychical phenomena are of importance in anesthesia. One of these is that an involuntary blindfolding, coupled with fear, causes a feeling of impending suffocation. This is true in the psychological laboratory as well as in the anesthetizing room. It is not a sense of suffocation that results, but a feeling of impending suffocation.

The patient just before or at the commencement of anesthesia does not complain of being choked, if minimum quantities of the anesthetic are administered, but he says: *"Doctor, don't choke me," "Doctor, you'll smother me."* It is something he feels is *about to come—not a sensation that is present.* If this idea is allowed to form, or to persist if formed, the patient will grab the inhaler or struggle to get away from the anesthetist, and as the anesthetic takes a firmer hold on him complications will arise, and to what extent these associations may go the anesthetist cannot tell.

The patient's eyes then should be left uncovered during the induction. He should be allowed to use them just as he pleases. Since using an inhaler that cannot cover the patient's eyes I have never had a patient complain of impending suffocation.

The last psychic condition to which I ask attention is the horror people have of taking an anesthetic the second time. This is because of the unpleasant concomitants of the former anesthesia. Of course, the way to prevent this postanesthetic antipathy is to have the induction of the anesthesia free from all unpleasantness. The phenomena preceding and incident to induction of anesthesia remain prominent in the minds of patients for years, even when all else connected with the operation has passed out of the mind.

The reason is multiple. First, there is a feeling of dread—dread of the anesthesia, dread of the operation. Then there is the feeling of fear—fear that something may go wrong, fear that the findings of the operation may be unfavorable. Then there is the feeling of complete helplessness. The patient feels he must give himself into the hands of strangers who can do with him as they please; that he himself will have no control over the situation. Then there is that feeling which of all is to many patients the worst, namely, the feeling of voluntarily closing their eyes on the world with the possibility of never opening them here again. All of these ideas make the mind peculiarly sensitive and the most insignificant impression at this time is a lasting one.

Therefore, every effort should be made to render the induction as free from unpleasant

circumstances as possible. I have already explained the rationale of success in accomplishing this so far as psychic methods obtain. The only additional point that it is necessary to make refers to the part of the actual administration of the anesthetic, the full details of which lie outside the province of this paper. This point, necessary here, is that at first the anesthetic should be administered very slowly. The induction should be gradual. If the anesthetic is ether there should be no limitation of respiratory air and the ether should be dropped onto the mask very slowly. By doing this the membranes of the respiratory tract will become locally anesthetized so that later the ether may be dropped rapidly for a speedy induction without any irritation from the ether. If this and the other methods of procedure which I have explained are carried out, few patients will shrink from a later necessary anesthesia.

THE PROPER ADMINISTRATION OF AN ANESTHETIC IS MORE THAN A MERE MECHANICAL PERFORMANCE, IT IS AN ART. THE ART OF ANESTHESIA IS ACQUIRED BY BECOMING FAMILIAR WITH THE LAWS WHICH GOVERN ITS ADMINISTRATION AND BY DEVELOPING THE ABILITY TO PROPERLY CORRELATE AND APPLY THESE LAWS.

IT WILL BE PERCEIVED THAT WHILE A KNOWLEDGE OF THE LAWS IS ESSENTIAL, YET THIS KNOWLEDGE IS SUPERSEDED BY THE ABILITY TO PROPERLY APPLY THEM. THIS CONTROLLING ELEMENT IS WHAT CONSTITUTES THE ESSENCE OF THE ART. EXPERIENCE BEGETS DEXTERITY, TACT AND SKILL. THESE QUALITIES, WHILE SOMEWHAT INTANGIBLE, ARE NEVERTHELESS INDISPENSIBLE. THEY IMPLY A CORRECT AND SPONTANEOUS RESPONSE TO THE DEMANDS OF THE PATIENT.

THE ART OF ANESTHESIA IS NOT CONTAINED WITHIN ANY PARTICULAR MODE OF ADMINISTRATION. SO-CALLED EMPIRICAL, PERCENTAGE AND SHOCK-ABSORBING METHODS HAVE THEIR PLACE, BUT SHOULD NOT BE PERMITTED TO DOMINATE OVER THE ART IN ITS BROADER SENSE. THEY ARE ITS TOOLS AND MUST BE OBSERVED FROM THE POINT OF VIEW WHICH CONSIDERS THE SURGEON, THE PATIENT, THE PLACE AND MANY OTHER FACTORS.

SINCE FAMILIARITY BREEDS CONTEMPT, THE ANESTHETIST MUST NEVER FORGET TO APPROACH EACH CASE WITH A CERTAIN DEGREE OF COURTESY AND RESPECT, FOR THE POSSIBILITIES OF SUCCESS AS WELL AS TROUBLE IN EACH ARE ALMOST UNLIMITED. A THOUSAND ANESTHESIAS, INSTEAD OF LEADING TO CRUDENESS, SHOULD MAKE ONE A THOUSAND TIMES MORE CAREFUL. AS ONE PROCEEDS, ONE SHOULD TRY TO FORMULATE LAWS AND THESE ONE SHOULD TRY TO PROVE BY THE NEXT CASE.

TO GIVE AN ANESTHETIC IS ONE THING, TO PRACTICE THE ART OF ANESTHESIA IS ANOTHER.

—Paluel J. Flagg.

THE USE OF MUSIC DURING ANESTHESIA AND ANALGESIA . THE ANESTHEASIEST WAY . OPERATING ROOM ATMOSPHERE . AVAILABILITY OF THE PHONOGRAPH . PREPARATION OF PATIENTS . SELECTION OF MUSIC . METHODS OF USE DURING OPERATIONS, THE INDUCTION OF ANESTHESIA, RECOVERY AND CONVALESCENCE . CONCLUSIONS.

BY W. P. BURDICK, M. D., KANE, PENNSYLVANIA

A BRIEF LETTER which appeared in the correspondence column of the *Journal of the American Medical Association,* issue of June 6th, 1914, and signed by Dr. Evan O'Neil Kane, of Kane, Pa., was productive of rather interesting results. The letter referred to the use of phonograph music in operating rooms; and the new idea was so opposed to the fixed ideas on the subject of operative procedure that paragraph writers, and some doctors, used it as a safety valve for their pent up wit. Their attitude demonstrated once more the fact that the introduction of any new thing is sure to arouse the skeptic from the lethargy that sometimes overtakes him.

The suggestions which were made by the humorists as to the musical selections which would please them most, and be best adapted to the case when about to go *under the knife*, brought out an important principle which it is absolutely necessary to make use of in the successful adoption of music as a means of mitigating the dread of operations. If Mankind were always consistent, the idea of suitable music as an accompaniment to surgical clinics would seem entirely rational.

Theology teaches that the person who lives up to the principles of Christianity in this life passes, at death, to a higher, nobler and far happier existence; and yet, as practically all concede that *no traveler* has yet returned to verify these statements, even the most faithful Christian may be excused if at times there is a slight wavering of faith when facing dissolution; and an expressed willingness to bear, for awhile longer, at least, the ills they have.

But modern surgery offers to suffering humanity not only hope, but statistics. Few, indeed, are they who do not know that the skilled surgeon of to-day is able to eliminate most of the very worst afflictions that affect the human race; and that in the great majority of cases those who submit to surgical interference are restored to health, and a life of usefulness.

Assuming that the patient is free from mental bias, and is capable of taking a common-sense view of the situation, the fact that he or she is about to be relieved in one brief hour of some abnormal growth or condition that time and medicine could not cure, and which caused years of suffering and abject misery—this fact should cause great rejoicing. Instead, however, the patient is usually bidden a tearful farewell by the family and friends, and enters the operating room atmosphere often with such feelings of horror and dread as to be on the verge of collapse.

By *operating room atmosphere* I mean the demeanor and low professional tones of the surgical staff, the expressionless faces and whispers of the nurses, or an almost complete silence that is quite often harshly jarred by the rattle and banging of instruments. Realizing that these things are wrong in practice as well as in theory, we have, at the Kane Hospital, been endeavoring in some manner to break away from then, and surround the patients with more natural conditions—the more effectually to reassure them, and dispel their fears.

The installation, then, of a phonograph ac-

companiment to our operative work in the operating room was not a mere erratic experiment. It was suggested as a result of experience with appeals to the musical sense among individuals elsewhere. For some time a phonograph had been employed in the wards of the hospital as a pastime for the sick. It was operated by those who were able to be up out of bed for the diversion of the less fortunate. These, with but few exceptions, took great delight in it. It was observed that even the most serious cases did better while the phonograph was in operation, although it was kept going continuously from early morning until after nightfall.

Though it had been objected that the instrument would interfere with sleep, this was not the case. Quite the reverse. Even recently operated cases, from the time of entrance into the wards, and while still coming out of the anesthetic, would be beneficially influenced. Fully 95 per cent. of all patients expressed a desire to hear the phonograph, and of the remaining 5 per cent. not more than about 2 per cent. made any serious objection.

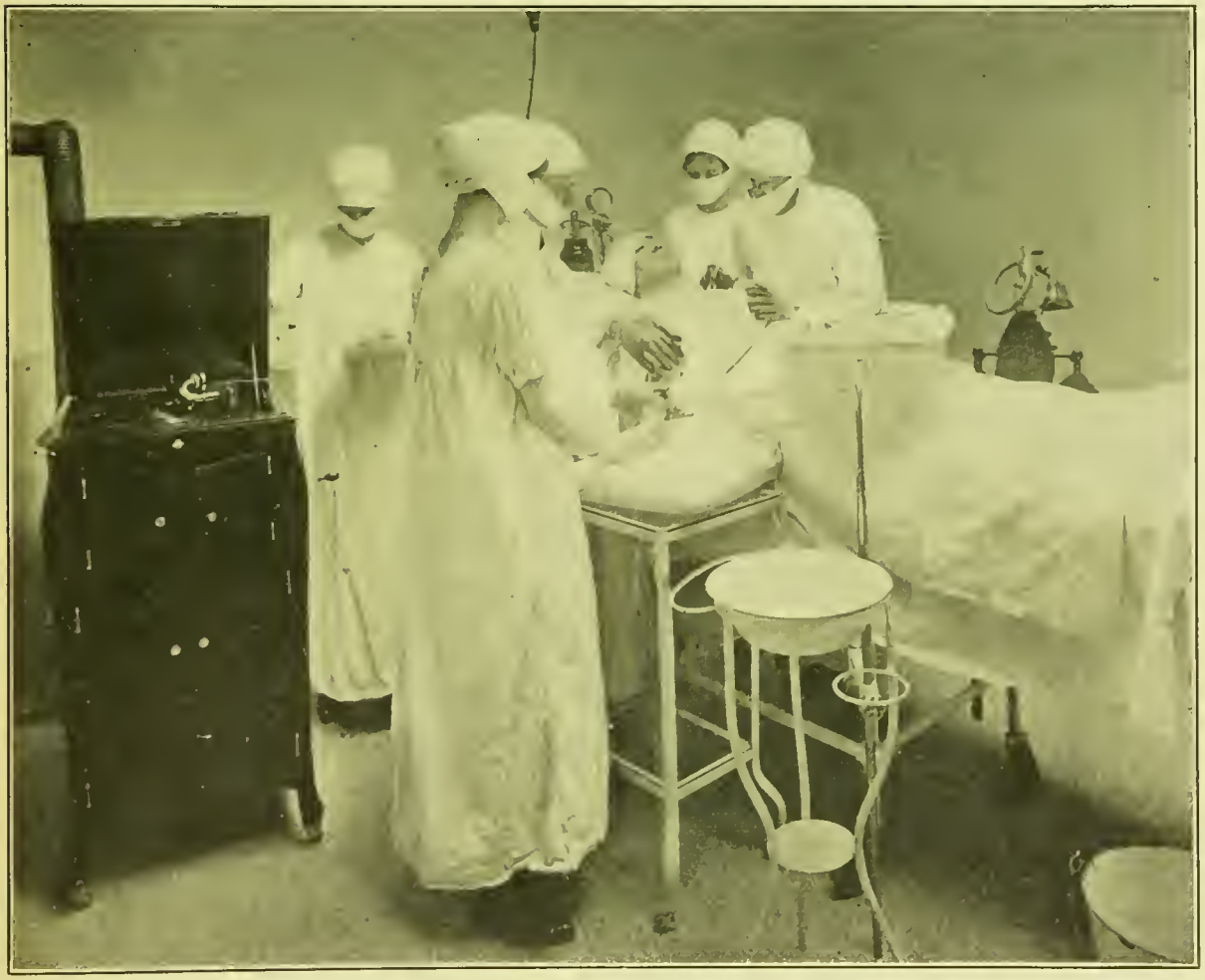


Figure 1. Showing the use of the phonograph during an operation under local analgesia in the surgical clinic of the Kane Hospital.

The striking facts above mentioned pertaining to the salutary influence of this instrument suggested to Dr. Kane and myself the idea of utilizing music as a diversionary means during operation under local analgesia. A phono-

graph was installed in the operating room, and pieces, instrumental and vocal, suited to the taste and temperament of individual cases, were selected.

My present method is to visit the patient on the evening before the morning of the operation, and in a little *heart to heart* talk I try to impress the fact that what is to be gone through with in the morning is by no means to be considered a trying ordeal. They will not suffer or be made uncomfortable in any way, but, in all probability, will be relieved of their affliction. I state that so far as considering the operation a grave affair (and by grave, in this case, I mean the opposite of gay), we look upon it with such cheerfulness that we frequently have a little music while operating. I learn the patient's nationality, and the degree of fondness for music; and when the subject is brought into the operating room to be placed upon the table, the machine—*muffled*—is playing in subdued tones some piece the patient had previously expressed a liking for.

There never has been any feeling of hilarity,

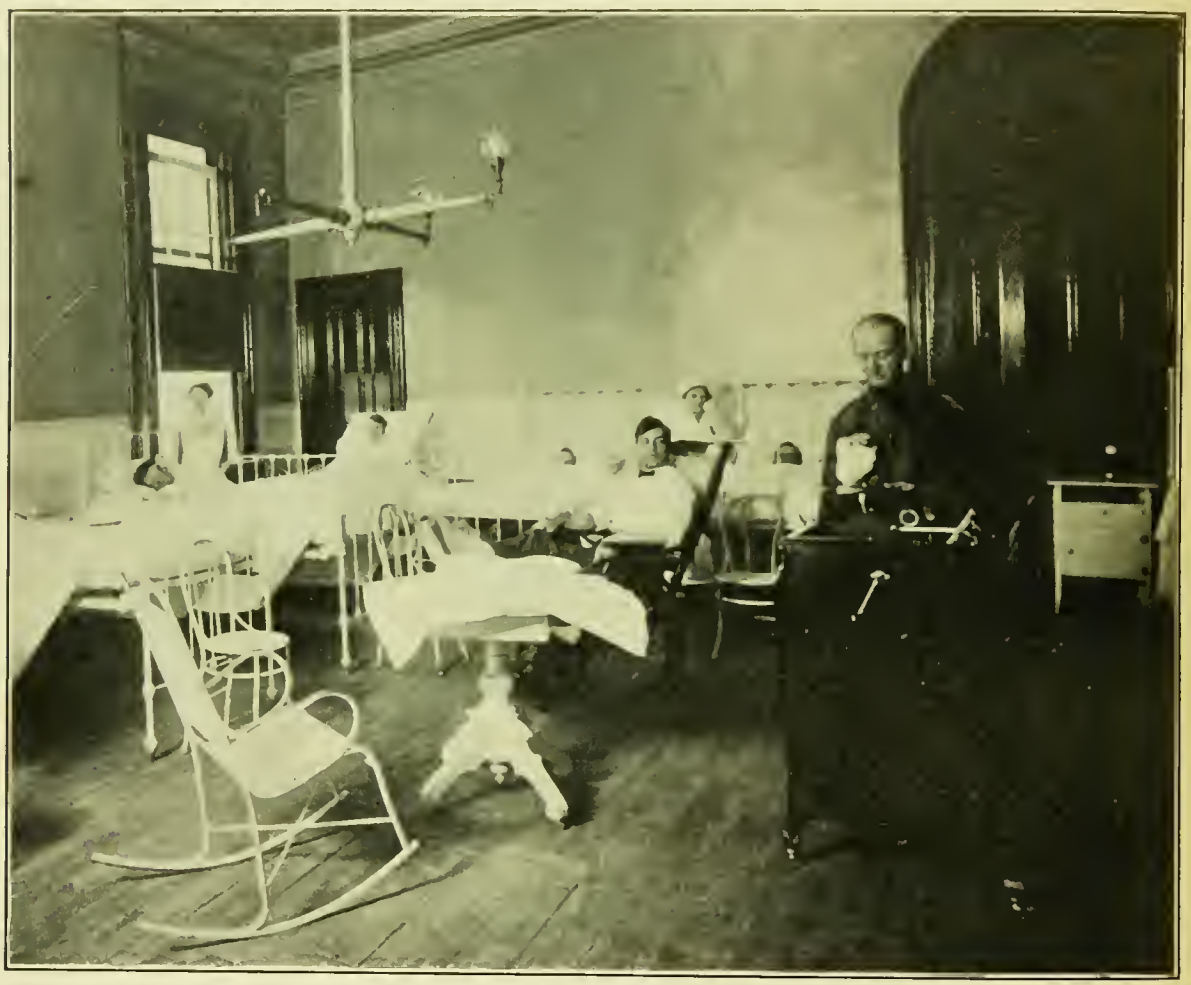


Figure 2. Showing the use of the phonograph in the wards of the Kane Hospital during convalescence.

for I think we all feel as did Jessica in The Merchant of Venice when she said: *"I am never merry when I hear sweet music."* We soon adapted ourselves to the innovation, and had no feeling that it was out of harmony with, or unsuited to, the occasion.

The effect has been highly satisfactory. In practically all cases the patients were attracted

by the songs and instrumental music, and were diverted from the operation from start to completion. It was no longer necessary to keep myself or assistant engaged in conversation with the patients to divert them. They had enough to occupy them. At points in the operation when the surgeon had to block a nerve, drag upon a viscus, or explore a peritoneum beyond the obtunded area, a sign from him was sufficient, and the attention of the subject was called to some tone, strain, musical theme or turning in the concert. Thus, without breaking the harmony of the operating room technic, the good offices of the *great god Pan* were invoked and gratefully accepted.

Next, it was suggested, from the pleasure the ward phonograph gave patients being prepared for operation, that the instrument be set in motion as the patients were being brought into the operating room to be put under general anesthesia, in order to antagonize the feeling of fear and horror so common during this distressing phase of the operative ordeal.

About this time, also, my attention was attracted by the remark of a female patient while *going under* gas. Our operating room is situated in the top of the building—four stories above the noise, dust and odors of the street. On the first floor is a large parlor; and on this occasion the soft strains of a piano floated up through the corridors from this room, and faintly penetrated the operating room. After two or three spasmodic whiffs of gas the patient said, in tones of extreme satisfaction: *"Oh! I hear a piano. How sweet, and far away it sounds;"* and immediately I observed that the tension was gone; the breathing at once became regular, and the patient quietly, and rapidly went to sleep.

We then placed the instrument just outside the room for general anesthesia, with the tones always muffled, and it served the purpose well; for we observed that the anesthesia was almost invariably taken more calmly, and with less tendency to resist the earlier inhalations than formerly. Also, and this was of no small importance, if the action of the machine was resumed for a few minutes as the patients were recovering consciousness, they were thereafter deluded into a dreamy idea that they had heard the strains of music from start to finish, without break in their connection; and consequently, had escaped all operative interference, the cure effected having been as it were extraneous to any operative procedure; *"lifted to Heaven," "translated," "borne to spirit land," "to limbo,"* and other and similar expressions being frequently used.

Not all patients could, as has already been suggested, be treated with the same instrumental, or vocal themes. Temperament, education, religious training, and other pyschic influences, as well as racial tendencies, have all had to be considered in making a real live success of this novel procedure. Otherwise it would be worse than a failure. The instrument, too, must be no *hand-me-down*, but one of the best; and only high-class music may be employed.

A few who are not benefited by the *song-world trance*, as Dr. Kane (desiring to keep pace with modern nomenclature) aptly puts it, make known their indifference to its charms so promptly, and with such emphasis, that there is no difficulty in discovering their deficiency in this respect, and the concert is brought immediately to a close, without further parley, and no injury is done.

Finally, the able physician, and the master surgeon, must, almost of necessity be lovers of the arts; for surgery has long been recognized as an art as well as a science. The same may be said of the practice of medicine in its truest sense. The very qualities, therefore, which make for success in the medical profession, lead one naturally to take an exceptional interest in other arts. Good music, then, appeals as a rule to an operating staff. It acts as a soothing medium during long, harrassing operations, and by lessening nerve strain and anxiety, conduces to better work, thus scoring another gain for the patient.

FROM THE OUTSIDE LOOKING IN . OLFACTORY ESTHETICS IN DENTISTRY . INFLUENCE OF MUSIC . CHARACTER AND HABITS . THE MIRACLE OF NITROUS OXID-OXYGEN ANALGESIA . THE TROUBLESOME SEX, AND HOW IT MUST BE DEALT WITH ACCORDINGLY.

BY JESSIE A. JARVIS, PORTLAND, OREGON

I BELONG TO A FAMILY of professional men. My husband is a physician; my brother is a dentist.

For fifteen years I have been an interested listener to discussions regarding new fields of research. The science and art of dentistry and medicine and the patient as viewed from the standpoint of the practitioner. I have quite grown to share in my husband's joy over finding *a beautiful mitral murmur* and to view with interest a case of trifacial neuralgia that has withstood treatment for an unholy length of time.

I can accept intelligently the statement that appears sardonic to the lay mind: *The operation was successful but the patient died.*

It was while listening to a discussion of an operation of this latter variety that it occurred to the writer that it might not be amiss to present to the profession a short paper that would show the opposite side of the picture, namely that of the practitioner from the standpoint of the patient.

I have suffered all my life from the fragile, sensitive teeth that are the natural outcome of a nervous and delicate childhood; but some inbred abhorrence of what our country cousins call *store teeth* has led me to endure all things to preserve them to myself with the result that I have spent much of my existence in a dentist's chair.

I believe it is said with authority that our olfactory sense is the one most strong in the power of association. As you go into the average dental office what is the first thing that strikes your senses? Is it not safe to say carbolic? For myself I do not object to the odor; it is cleanly, antiseptic and not sickening, but it is not suggestive of the normal, happy things of life. Perhaps a hint of creolin is a close second, which to every lover of canines spells *dog soap*. As I belong to the class of doggy-people, again I am not greatly annoyed, but there are many women who will be actually sickened by the smell.

So used have we become, through long years of custom, and so strong is the power of anticipation that it takes more than the mere absence of these things to persuade one that they are not there.

I have in mind an office almost unique in my experience where you are greeted the minute you enter by the fragrance of flowers; in early spring you will find great bowls of pink and white lilacs; later when June brings her roses, the place is a bower of fragrant beauty. Even in winter when the hot house is the last resort, there will be spicy carnations, a few great, ragged, red blossoms in an Arts and Crafts vase against a dull green wall.

There are few people who, consciously or not, will fail to be quieted by such an influence; and relaxation will to an extent replace the high tension of anticipated suffering.

There is an office in Philadelphia with which I am very familiar. The rooms are large and sunny and filled with big easy mission chairs of the best form and finish, a large divan holds enough leather pillows to suggest a veritable cozy corner, but the thing that first attracts your eye upon entering is an open piano with a violin resting on top. This man is a really thorough musician and has continually under his guidance a succession of boys and girls, young men and women who are working hard to get on their feet in the musical world. He

is too busy to give his time and attention to those who can never rise above the rank of parlor performers, but he opens his home to those who show true genius and they are welcome to come and practice in his office; not technical exercises, but rare parts of their work that will give pleasure to the listener.

The old adage, *Music hath charms to soothe the savage breast,* is as true today as when it was written and it is certainly easier to endure pain when listening to *Bach's Aria* or the *Berceuse from Jocelyn* when played by a violinist or pianist of promise.

Do not understand me to mean that these agreeable and diverting surroundings ever take the place of fundamental cleanliness.

We have all, I believe, at some time experienced the shock of meeting a beautifully dressed and daintily perfumed woman and being completely disillusioned by a chance glimpse of untidy lingerie or other negligence.

At the present day every intelligent woman demands cleanliness that shall be not only comparative, but absolute; whether this be inherent, or the result of education and environment, the great fact remains that she will have it and will not be satisfied with her dental work until she finds a man who comes up to her requirements.

Not only is this true of the cultured class, but as we descend rung after rung of the social ladder, it is surprising to note the amount of information possessed by our humble sisters regarding germs and microbes.

Their sources of information may be dubious and some of their conclusions truly weird, but the demands they make are practically the same as those we find in higher life.

There is in one of our large cities a young man who bids fair to be one of the *big men* of dentistry. His work is above reproach; he is cultured and attractive; his offices are the last word of good taste and comfort; his practice is drawn largely from the social people who form his social set.

A short time ago a lady who was a newcomer to the city asked me to recommend to her a dentist; she was well-to-do and had the fragile teeth that mean a steady patient. Her ten-year-old son was a subject for orthodontia. I gave her the name of the man in question, feeling sure that I had brought the right people together. A few weeks later we chanced to meet and I asked her how she had been pleased with her work. She said: *"Undoubtedly he knows his business but he was so reeking with tobacco that I couldn't stand having him near me."*

To the present day that young man is wondering why he lost that very desirable patient.

So closely allied to this matter of personal cleanliness that the two should go hand in hand, is that of the corresponding moral attribute. If one can say of a dentist, *"he is a good man not only in his professional, but private life,"* the practice he builds will rest upon pillars that will give it a permanent support.

Mothers do not wish to trust their young daughters to the care of a man, whatever his ability may be, whose reputation is not like that of Caesar's wife. Pass in review the career of any man who has had a long and enviable practice, or consider that of any successful practitioner of today, and you will find few exceptions to this rule, that they are men not only skillful and honest in their work, but deserving of the absolute loyalty and trust of the people who come under their care.

I do not wish to close this paper without relating an experience I passed through a few months ago that seemed to me little short of miraculous. I have suffered so many things for so many years in the effort to preserve my teeth that when one day my dentist, who is also a friend of long standing, came in to tell me that he was at last able to work on the most sensitive teeth without pain, I was frankly skeptical. So anxious was he to give me a demonstration that I hastened my regular semi-annual visit for a general inspection by a few weeks, and there as if made to order was a cavity in the most suitable possible place, one of the central incisors close to the gum. The bare pressure of the instrument against the tooth was almost unbearable and I realized afterwards that I was purposely subjected to that pain that the subsequent relief should be more apparent. It was nitrous oxid-oxygen that performed what seemed to me wizardy. The apparatus was adjusted and after a few seconds of its influence I found that while I retained consciousness I was absolutely numbed to any feeling of pain. I knew that the bur was being used,

that it was cutting deep and hard, but so entire was the paralysis of sensation that I felt as if I must be under the influence of a complete analgesia.

I was allowed to return to normal when the filling was being prepared and then a few minutes more of the nitrous oxid-oxygen and the work was done. I left the office almost dazed with the experience I had passed through and feeling as if I must tell everyone that the barrier of pain in the realm of dentistry had at last been overthrown.

I can affirm confidently that anyone having one such experience would travel a long distance before subjecting themselves again to the time-honored methods of treatment.

I am well aware that I am a member of the troublesome sex; many of us are nervous, too many of us are hysterical; we do not bear pain well and we are always looking for flies in the ointment, but such as we are, we are, and must be dealt with accordingly.

Our general attitude of mind I believe has been fairly set forth in this paper as by one who sees both from the outside looking in and from the inside looking out.

THE ART OF ANESTHESIA IMPLIES AN INTIMATE KNOWLEDGE OF GENERAL MEDICINE, PATHOLOGY, SURGERY, THERAPEUTICS, PSYCHOLOGY AND SPECIAL BRANCHES. THOSE WHO ARE NOT FAMILIAR WITH THESE SUBJECTS CANNOT UNDERSTAND THE LANGUAGE OF ANESTHESIA.

FOR EXAMPLE, HOW CAN A LAY PERSON INTELLIGENTLY FORM AN OPINION UPON SUCH VITAL MATTERS AS ACIDOSIS, TOXEMIA, CARBON DIOXID, STIMULATION AND DEPRESSION? HOW CAN HE UNRAVEL AND RELIEVE THE UNTOWARD SYMPTOMS WHICH MIGHT ARISE IN A CASE COMPLICATED BY RESPIRATORY OBSTRUCTION, MORPHIN DEPRESSION AND REFLEX INHIBITION? ASIDE FROM THE TIMIDITY OF INTELLIGENT PEOPLE TOWARD THE TAKING OF AN ANESTHETIC, THE SURGEON CAN ILL AFFORD TO LET THE PUBLIC KNOW THAT HE IS WILLING TO RISK THE PATIENT'S LIFE AT THE HANDS OF AN ANESTHETIST WHO IS NOT A MEDICAL MAN. DOES NOT THIS VERY EVIDENT LACK OF CONCERN IMPLY TO THE MIND OF THE THOUGHTFUL PATIENT A GREATER LACK OF CARE WHICH MAY INCLUDE THE OPERATIVE PROCEDURE.

A LAYMAN WHO ADMINISTERS AN ANESTHETIC IS LIKE A BLIND GUIDE WHO IS LEAD BY THE PATIENT, INSTEAD OF LEADING HIM. UNABLE TO PROPERLY APPRECIATE OR ANTICIPATE THE STAGES OF AN OPERATION HE CANNOT JUDGE THE INDICATIONS FOR ARTIFICIAL STIMULATION. THOSE WHO RELEGATE ANESTHESIA TO THE LAYMAN, PLACE THE RESPONSIBILITY OF THE OUTCOME ON THEIR OWN SHOULDERS.

—*Paluel J. Flagg.*

KIDNEY FUNCTION UNDER ANESTHESIA . THE COLLOID-CHEMICAL BASIS OF KIDNEY FUNCTION . LIPOID-SOLVENT ANESTHETICS . PERSONAL INVESTIGATIONS . ACIDOSIS . INDICATIONS . METABOLIC DISTURBANCES . PREPARATORY, OPERATIVE AND POSTOPERATIVE REGIME . CARBOHYDRATES, ALKALIES, FRUIT-JUICES AND SUGAR . DEHYDRATING EFFECTS OF SUGARS IN INFECTION-TOXEMIA.

BY JAMES J. HOGAN, M. D., L. R. C. P., SAN FRANCISCO, CALIFORNIA

IN ORDER TO understand clearly the changes in urinary output which follow anesthesia it is necessary to detail first some of the factors that help to maintain a normal secretion.

Modern writers like Hans Meyer and Gottlieb[1] hold that we are still far distant from a complete understanding of the mechanism of urinary secretion on purely physico-chemical grounds. While strictly speaking this is no doubt true, it is questionable whether there is anything gained by slipping back into the older teachings of the Heidenhain School and saying that a kidney secretes because it is able to. Certain it is that the last decade has helped to a better formulation of the physico-chemical conditions which are the sine qua non for secretion, and equally certain is it that the gains thus made may be used to advantage clinically.

Martin H. Fischer[2] has given us on a colloid-chemical basis a clear and logical explanation, supported by uncontroverted experimental facts, of the mechanism by which the body holds under varying conditions not only a normal amount of water but also such abnormally large quantities as are characteristic of edema.

He holds that the water in the body is not free, but is held as hydration water in combination with protein colloids; and that the body cannot take up any more water or give off any except as the state of these colloids is first changed. Water does not become available for urinary secretion, therefore, except as it is first brought to the kidneys in a free state.[3] The blood and tissues hold under normal circumstances what we call a constant amount of water. Water taken into the body in excess of the amount necessary for this saturation remains free in the blood and is excreted in some form, as from the skin, the lungs, the bowel, or as urine. The amount of water held by the blood and tissues is determined by the state of their colloids, which in turn is dependent upon the amount and kind of acid, alkali or salts contained in them. Thus, if their acid content is raised, more water is held by the tissues, in other words, an edema follows. When more water is thus held, less free water remains over to be available for secretion.

While an edema may effect any organ, it is a more serious state in some than in others. An edema of the brain is more serious than one of the skin, for example. Especially may an edema be serious in its effects if the involved organ is hampered in its swelling. Such hampering makes things worse, for the swelling organ then tends to shut off its own blood supply. This is true, for example, of the kidney, which being surrounded by a firm capsule, can only swell to a limited degree before it begins to shut off its blood supply. With the lack of oxygen thus produced, a diminished kidney function, (as betrayed by a diminished urinary secretion) becomes progressively worse and may go on to complete suppression, *anuria*.

We are indebted to Hans Meyer and E. Overton for explaining why narcotics, such as anesthetics, while capable of affecting all

living cells, produce their greatest effects in the higher animals upon the central nervous system. Because of their greater solubility in the fats and fatlike bodies—*the lipoids*—they accumulate in greater concentration and more quickly in the central nervous system and the adipose tissue than elsewhere in the body.

The best explanation of *why* they act anesthetically is given by Verworn. This author has shown that anesthetics enter into loose physico-chemical combinations with the lipoids, wherefore these lose their normal relation to the other cell constituents. As a result, the entire chemistry of the cell is inhibited. Among the results of this inhibition is a lessened absorption or utilization of oxygen. But whenever the oxygen supply to any cell or organ is thus cut down an abnormal increase in its acid content results. But such, in its turn, by increasing the capacity of the involved tissues for water is followed by edema. It is this edema which makes the anesthetized subject after the anesthesia feel *dry* and call for water. The very fact that the patient is thirsty and that his tissues are therefore not saturated with water means, of course, that there can be no free water in the body. This fact is betrayed through the kidneys, which show it by a diminished urinary secretion.

The chemical effect of the anesthetic upon the chemistry of the whole body evidences itself in certain qualitative and quantitative changes. There is, for example, an increased hydrogen ion and titration acidity observable on examining the urine and a diminished chlorid output. At the same time the presence of incompletely oxidized bodies, as acetone and diacetic acid and betaoxybutyric acid, may be found. If the resultant acid intoxication is severe, albumin and casts appear in the urine and an increased ammonia elimination may be observed. The presence of albumin and casts means that the acid intoxication has gone so far in the kidney that parts of it have gone into solution. The presence of acetone and diacetic acid means that carbohydrate and fat metabolism has been so upset that they are not completely oxidized, as normally, into carbon dioxid and water. The retention of chlorids by the tissues goes hand in hand with increased acidity and is due to this acidity. An increase in the acid content of a tissue not only leads to a retention of water—*edema*—but to a retention of certain salts at the same time.

These considerations show that *urinary secretion is possible only when free water circulating in the blood is brought to the kidney, and that an anesthetic produces the effects it does because it leads to a lack of oxygen in the tissues of the body. This raises their acid content, and makes them absorb more water from the blood, which in its turn diminishes in that proportion the amount available for secretion.* The kidney secretion diminishes not because of a specific poisonous effect of the anesthetic upon the kidney alone, but because of this effect upon all the tissues and organs of the body.

During the latter part of 1913, assisted by Grace McKenna, I examined 400 post-operative urines at the St. Francis Hospital in San Francisco. I found 94.2 per cent. of the cases to show a marked increase in the hydrogen acidity. Forty-nine per cent. showed acetone or acetone and diacetic acid. Twenty-six per cent. showed albumin and casts. Whenever these findings were noted there was also found a low chlorid output. In the great majority of cases only a trace was excreted. The surgical series embraced about everything for which operations are made. The average time per operations was 55 minutes; the average amount of ether given, 120 c.c. The post-operative symptoms of nausea, vomiting, headache, and gas pains paralled completely in their intensity the intensity of the changes noted in the urine.

This very evident parallelism between degree of acid intoxication and certain post-operative findings which have been and still are regarded as largely unavoidable and necessary consequences of operative interference suggested the probability that much could be done to make these patients not only better surgical risks, but also to make their post-operative history freer from complications than is now the case, if only some well recognized physiological facts were utilized in surgical practice. This has been found to be possible to a remakable extent, not only in my own cases, but in those of some of my colleagues. We have made it a rule, where emergency did not interfere, to discover in all cases before operation how heavily *acidosed* our patients are, and

then not to operate until through proper feeding and by the administration of alkalies such acidosis has been overcome.

In this connection it should be clearly borne in mind that much clinical misinformation exists in clinical and surgical circles to-day as to the question of when a patient is really *acidosed*. This word should be used as synonymous with *acid intoxication*. An acid intoxication is revealed by a persistently high hydrogen ion acidity,[4] or titration acidity of the urine,[5] by a high ammonia coefficient,[6] by a low carbon dioxid concentration in the blood or expired air, and by an inability to hold the breath as long as normally.[7] Ordinarily it is said that the appearance of acetone, diacetic acid, and betaoxybutyric acid is evidence of *acidosis*. This is not the case. It is *qualitative* evidence of a disturbed body chemistry from which an acid intoxication may result, but obviously, an organism may be poisoned to death with even the *normal* acids formed in body metabolism, while, on the other hand, even a great production of *abnormal* acids may leave the body uninjured, if only enough alkali is constanly available to neutralize the acids as formed.

These facts have been utilized as guides to a more scientific preoperative preparation of the surgical patient and his subsequent postoperative cure. Most preoperative preparation used to be, and in some cases still is, of a type to guarantee from the outset a maximum of discomfort and even danger to the patient. Routine examination of the patients to be operated on, even when not suffering from infections or intoxications likely to be complicated by nephritis, show that in the days before their operations they are usually pushed into a state in which postoperative complications are very likely to appear. Commonly the urine shows a high hydrogen ion concentration. Such patients make poor surgical risks, and should be given the advantage of preliminary treatment. The mental anxiety so common in surgical cases expresses itself physiologically by increased muscular tone, and this declares itself in the high acid findings in the urine. How much the intelligent reassurance of the surgeon must mean to such patents is obvious.

Patients are also too commonly ordered upon a *light* diet. In this way the acid products of a starvation diet are added to those already present from other sources. Unless there are specific reasons against it, a surgical patient should be fed to within six hours of his operation, and since carbohydrate starvation is the commonest and earliest form, special attention should be paid to getting an easily assimilable sugar-starch ration into him.

I usually order the protein intake cut down somewhat, and put in its stead more carbohydrates. The use of mushes, oatmeal cooked for three hours and served with plenty of sugar, malted milk, or any of the prepared foods that contain maltose and dextrose in an easy assimilable form does very well.

In addition the patient should be given *water,* as urinary secretion is only possible by furnishing a sufficient quantity of free water. It must be remembered that large quantities of pure water alone tend to wash the salts out of the tissues. This may be met by combining with the water salts up to a *physiological* concentration, and alkalies. Natural or artificially prepared mineral waters are particularly easily borne by the patient and when these contain a maximum amount of calcium they are particularly satisfactory, for a lack of calcium seems to be responsible for many of the so-called acidosis effects. The amount given should be regulated by the urinary reaction. I see that my patients reach the operating table with their urine alkaline to litmus or rosolic acid, and passing at least 1,500 c.c. urine a day. If a water containing calcium is not readily available, I give calcium acetate in gram (15 grains) doses three or four times in the twenty-four hours in addition to whatever water I use.

The feeding of carbohydrates and the use of water, alkali, and salt should be started, if possible, at least two or three days before the anticipated operation either at home or in the hospital, and continued until the patient has a urine persistently neutral to litmus or rosalic acid. He should enter the operating room in this condition. A patient who goes to the operating table with a highly acid urine, or with a high ammonia coefficient, or with products showing a disturbance in his carbohydrate metabolism, *acetone and diacetic acid,* is a bad surgical risk.

I see that the bowels are moved just before

the operation. I use instead of the ordinary enema one consisting of a quart or two of water containing one or two ounces of bicarbonate of soda. The patient is allowed to reject in the ordinary way, but since all does not come out, a considerable dose of alkali is thus given the patient just before he is subjected to his increased surgical acidosis, the result of his anesthesia, his acid production from the pain of the operation, and his post-operative suffering.

Patients prepared as I have outlined recover rapidly from the effects of their anesthesia. They are without headache, *absense of brain edema;* they vomit little or none at all, *absence of edema of the medulla;* they urinate an hour or two after the operation, *absence of kidney edema and early presence of free water;* the urine is practically free from albumin and casts and excess of ammonia. Moreover, the traumatized tissues at the seat of the operation swell less and are less painful, due also to the decreased edema.

The choice of anesthetic should receive consideration. The toxic effects of an anesthetic, as far as the kidneys are concerned, deserve consideration from several standpoints. In the first place, no anesthetic, be this chloroform, ether, or nitrous oxid, can produce its desired effects without interfering with the oxidation chemistry of the body. In fact, anesthesia depends largely, if not entirely, upon such effect. We need not, however, add to this load by giving the patient too little oxygen. One of the superior merits of nitrous oxid anesthesia resides not so much in the anesthesia itself as in the fact that oxygen accompanies it. Nor may we say offhand that the bad effects of an anesthesia are simply a function of its length and the quality of anethesia used. Alvin Powell found in a carefully studied series of operative cases that when but little anesthesia was used, and perfect muscular relaxation was not obtained, the patients showed more casts and albumin in the urine than when they were anesthetized longer and more deeply. On the other hand, very deep anesthesia was again followed by more albumin and casts. I have noted the same facts in experimental work on rabbits.

These findings are to be interpreted as follows: The bad effects avoided by use of but little anesthesia are more than counterbalanced by those incident to the great acid production consequent upon imperfect muscular relaxation. The imperfectly anesthetized subject responds with muscular contraction to the irritation due to surgical trauma. A medium degree of anesthesia increases the toxic effect of the anesthetic, but eliminates the acid factor due to muscular rigidity. In deep anesthesia a maximum of interference with normal oxidation chemistry is again assured by the anesthetic itself.

Similar conditions hold in determining the value of morphin, atropin, scopolamin, and similarly acting drugs admnistered before or after an operaton. Their bad effects on the oxidation chemistry of the tissues may be offset by the assurance of better muscular relaxation, with the elimination of acid production from this source.

I always give scopolamin (gr. 1/200) and morphin (gr. 1/6) one hour before operation, as I find that less anesthetic is necessary under these conditions, and in a patient properly alkalinized with plenty of free water available for secretion there is no danger in this. By this means one obtains better muscular relaxation and hence less acid production which more than overbalances the bad effects of the narcotic alone.

The value of local anesthetic measures, in the use of novocain, quinin, and urea hydrochlorid, as in nerve blocking and tissue infiltrations, is similarly explained. Their use prevents pain impulses from reflexly expressing themselves in increased muscular tone. I infiltrate each layer with 0.25 per cent. novocain and block the area with 0.2 per cent. quinin and urea hydrochlorid.

By following such simple details the good surgical patient is not only kept so, but many a bad one bordering on an acid intoxication is not pushed over the line into a serious or perhaps fatal terminal state. Cheerful surroundings, confidence in surgeon and nurse, proper anesthesia, and the blocking of peripheral impulses keep the acid production in the body low, while carbohydrate feeding, alkali salts, and water push the danger threshold further away. The latter elements protect the body against the effects of the operation—the in-

toxication of the anesthetic and the acid effects due to post-operative suffering.

Following operation, the patient is allowed an alkaline mineral water either plain or as a fruitade. Early administration of the juice or pulp of grapefruit and oranges with sugar works excellently. The fruit acids are oxidized to carbonates so that these foods represent a feeding of alkali. If there is no vomiting I start carbohydrate feeding by mouth within a few hours after the operation. Sweetened fruit juices, hot or cold malted milk, and candy I find excellent.

In cases of marked toxemia, especially in victims of a subacute or chronic affection, more sugar than can be given by the mouth should be administered. In this type of case the rectal administration of 4.5 per cent. anhydrous dextrose by the drip method works very well.

Up to the present we have contented ourselves with dealing with the rôle of the acids in the production of edema in the different organs of the body. Recent experimental work by Martin H. Fischer and Anne Sykes[8] shows that urea, pyridin, and some of the amins lead to a marked hydration of proteins. This observation seems to be of fundamental importance in connection with the edemas associated with the infections, for many of the bacterial toxins are amin in character. The point of interest about the edemas produced by the amins is that they are different in type from those produced by acid, for while the latter are relievable by the use of bases and salts, those produced by urea and the amins are not thus influenced. On the other hand, the sugars, which influence acid edemas but little, dehydrate this second type of edema tremendously.

Martin H. Fischer and Anne Sykes[9] have also shown that the sugars dehydrate the body as they dehydrate simple proteins. The diuretic action of the sugars depends upon this fact and like the saline cathartics the sugars act as diuretics primarily, not because of specific action upon the kidney, but because they dehydrate the tissues of the whole body. The degree of diuresis increases with every increase in the concentration of the sugar.

Especially in the toxemic cases have I found the sugars to produce excellent results. The dextrose not only acts as a food and thus furnishes the necessary carbohydrate so often lacking in the body, but it is a powerful dehydrator. In this second capacity it reduces the swelling of edematous organs, such as the kidney, brain, liver, and bowel, while secondarily it leads to a liberation of water, thus increasing the urinary output. Clinically, I have found the rectal or intravenous injection of sterile, hypertonic anhydrous dextrose solutions—up to 18 per cent.—to produce most spectacular results in anuria, ileus, coma, persistent vomiting, and glaucoma.

In conclusion I hope that these observations may help the reader to a better scientific understanding of why sugars, alkalies, and salts which in one way or another have been used empirically for generations in the care of the surgical patient, really accomplish their purpose.

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THE MANUFACTURE OF NITROUS OXID FOR HOSPITAL USE . OUR EXPERIENCES WITH TOXICITY . EFFORTS TO SECURE PURIFIED GAS . SOLUTION OF THE PROBLEMS INVOLVED . COST OF MANUFACTURE AND INSTALLATION OF PLANT . ADVANTAGES . ADMINISTRATION .

BY A. R. WARNER, M. D. *CLEVELAND, OHIO*

AT LAKESIDE HOSPITAL, nitrous oxid gas has been used for anesthesia extensively for about eight years, and has been manufactured as a routine at the hospital for more than six years.

For the first four of these years, the gas we manufactured was not entirely satisfactory to any one, and at times was not without harmful effects. This was overlooked at first, partly because, on the whole, we had as good results as others, and partly because it was then believed that a certain amount of cyanosis was necessarily present during nitrous oxid-oxygen anesthesia, and that bad after-effects were in a measure to be expected. As our anesthetists developed more skill with this anesthetic, they were able to demonstrate to us that the cyanosis, the irritaton, and the symptons of toxemia following the anesthesia were present to a greater or less extent in all or in several patients on the same day, and that on other days there were no such symptons at all: they convinced us that the gas made in the hospital contained a variable amount of some poison. Commercial gas, although producing at times the same symptons of toxicity, seemed more uniform and distinctly less irritating. The difference was fairly constant, although our plant and methods of manufacture were the same as the commercial plants and methods known to us. On our worst day one patient of the gynecologic service died with all the symptons of a severe toxemia a few hours after a simple operation; one patient of the surgical service was severely poisoned, and three others suffered to a lesser extent. The predominating symptom of the poisoning was a cyanosis that no amount of oxygen could dispel. The hemoglobin was evidently damaged, and our surgeons learned that outdoor fresh air treatment was the most effective treatment. The condition, with the exception of the color, resembled carbon monoxid poisoning, yet unufortunately no spectroscopic examinations of the blood of these patients were made.

About two years ago, it became evident to all that nitrous oxid must be obtained in greater purity, or its use in the hospital abandoned. On the good days this anesthesia was so satisfactory to the surgeons, so unobjectionable to the patient, and made the operative cases so easy to care for in the ward, that it seemed ideal for hospital use. In our opinion these facts justified every effort to make it right. The best consulting chemists obtainable were called to examine the plant and methods. Each pointed out possible defects, and all agreed that better apparatus and methods could probably be developed by experiment. Each called attention to the great number of possible impurities. One of our trustees, Mr. H. M. Hanna, then offered to provide the funds necessary to run an experimental plant at the hospital, and I undertook to solve in such a plant the two following problems:

(1) To find a method for the manufacture of nitrous oxid of sufficient purity to be without poisonous effect.

(2) To devise apparatus by which this can be done as a routine in hospitals under hospital conditions.

The details of many experiments with new chemical processes and types of apparatus need not be presented. The entire plant was rebuilt several times. The net result of the first six month's work was only more uniform gas: we did not have the very bad days, yet the evi-

dences of toxicity continued. About this time we found that nitric oxid, even when present in large amounts was entirely removed from the nitrous oxid by confining in iron tanks or over water for a few hours. This explained the lesser irritation from commercial gas, which stands longer in the gasometers and is always shipped in iron cylinders. Commercial gas has always been free from nitric oxid, and our gas—sometimes used without standing long in the tanks—had not been. In these experiments we became convinced that the poisonous effects were, at times at least, not from the nitric oxid, which has been the generally dreaded impurity. We learned, too, that the effect of the poison was cumulative, and that a long anesthesia was the compounds and other nitrogenous substances which certified to the presence of ammonia or substances breaking down to ammonia. To test the hypothesis that these basic compounds might be the poison, a thorough washing with strong sulphuric acid was then added to the process of purification of the gas. for the purpose of removing all free basic radicals. On this day, now over a year ago—our gas became absolutely neutral in reaction, and the peculiar cyanosis and all other symptons of toxicity disappeared from our operating rooms, never to appear again when acid-washed gas was used. We did, however, see it in varying degrees each time that the installation of new apparatus in the plant made it necessary to shut down and use for a few days

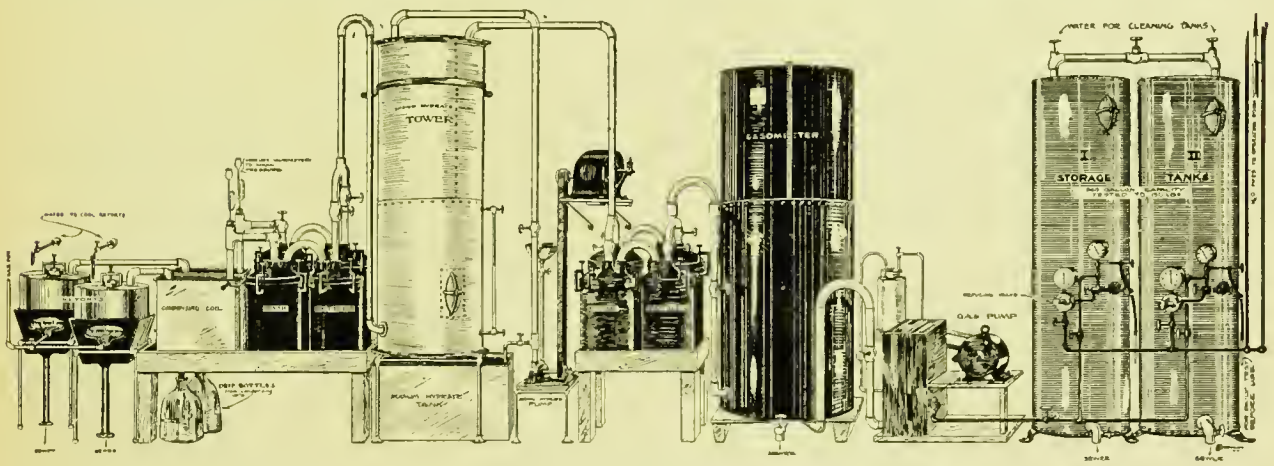


Figure 1. The Lakeside Hospital plant developed for the manufacture of purified nitrous oxid.

most delicate available test. In comparison with this, all analyses and chemical tests were crude.

The impurities theoretically possible to produce in the destructive distallation of even a pure ammonium nitrate in an iron or other reducing retort are many. Among these are many of the more highly organized, well-known hemoglobin poisons, as the hydrazins and hydroxylamins. It was at least possible that some of these were causing the trouble. Our gas and the best samples of commercial gas obtainable were tested, and all were found slightly alkaline to phenolphthalein. Published analysis of commercial nitrous oxid made by reliable chemists had reported the presence of traces of ammonium commercial gas not scrubbed with acid. All of our days are good days now: we are enjoying the advantages of this anesthetic without the disadvantages which had been so constant as to become regarded as necessary and belonging to it.

Confirming evidence came from independent sources. The Ohio Chemical Company of Cleveland noted our better results, and remodeled their plant. Three competent anesthetists, whom I have happened to meet, one from Boston, one from New York and one from Ithaca, volunteered information regarding the uniformly better results which they were having with the Ohio gas, all dating the better results from the date the company remodeled its plant and instituted the acid

wash as a part of the purification process. Later the Lennox Chemical Company remodeled its plant to include the acid wash. Since this date I have not heard of any evidence of toxicity or any bad results from the use of nitrous oxid in Cleveland or vicinity. These two plants manufacture all the gas sold in or about Cleveland.

The chemical work to identify the particular poison or poisons which have caused all the troubles has not been done. We know only that it is removed by the acid wash, and that it is found in the acid in the form of ammonium salts, which is consistent with the belief that it is one of the hydrazins or hydrxylamins. The problem of isolating the particular poisons by chemical means is too difficult to look attractive, now that the practical results have been attained without such work.

For the simple purpose of preventing commercial monopoly, applications for patents on a new method of separating the nitric oxid from the nitrous oxid, on a new wash jar devised, and on a process of removing the bulk of the impurities by condensing the 45 per cent. of water in the crude gas, as well as on the process of removing traces of alkaline substances, have been made. All patents issued will be held by the hospital to guarantee the unrestricted use of the apparatus and the methods covered by them.

To our mind the first problem has been solved. Nitrous oxid can be manufactured in sufficient purity to be absolutely safe for use in anesthesia. We are not yet quite sure about the second problem. Lakeside can now manufacture such gas as a routine, and safely, but the walls and ceilings of our room still bear marks made by pieces of bursted retorts, and our employees have not forgotten the fumes which repeatedly filled the corridors "from the gas plant." It is never entirely safe to place a pot containing a nitrogenous and an oxidizing substance over a fire. Many defects in the models of apparatus and troubles in the handling of the purification process have been overcome, some non-essentials have been eliminated, and safety devices have been added, so that it now seems to us entirely reasonable to expect a good chief engineer to supervise a similar plant and train a helper to run it; yet is remains to be demonstrated.

The cost of building a new plant for the manufacture, purification and handling of nitrous oxid similar to the one now in use at Lakeside would be about $2,700, and it would require about 600 square feet of floor space. This figure includes the cost of apparatus for liquefying the nitrous oxid and for filling small cylinders. The cost of apparatus for the handling of oxygen (purchased in large cylinders) outside the operating room, and for delivering it in pipes parallel with the nitrous oxid at the same constant pressure is about $300. This includes apparatus for filling small cylinders from the large. The cost of running the pipes for the nitrous oxid and oxygen to the operating rooms would be additional, and would vary with distance and difficulties. It would be the same as the cost of running water pipes the same distance.

COST.

From the first there has been a gradual reduction in the cost of nitrous oxid-oxygen anesthesia. Three years ago our costs were running about $10 per hour, divided into $3 for anesthetists' salaries and $7 for the gases and incidentals. The present figures are $2.50 for anesthetists and $1.57 for gases and incidentals, making a total of $4.07. In order to present the details of cost as clearly as possible, I have prepared two series of the detail of six consecutive months, each with averages. The first series ends with March, 1914, and the second with April, 1915. During the first series we purchased the small cylinders used, so that the amount of gas manufactured was not the total amount used. In the second period we compressed our own nitrous oxid for small cylinders, and filled small oxygen cylinders direct from the large. The filling of the small oxygen cylinders from the large is distinctly a saving. In Cleveland, the price of oxygen in small cylinders is just seven and one half times as much per unit volume as in large cylinders. This is due to the fact that the large cylinders, at least, are oxygen from the Linde process, which is apparently of perfectly satisfactory quality. The small cylinders are either refilled or oxygen from the old process. The figures for the amounts of the gases used are from the storage tanks in the basement, and therefore account for all leaks, accidents and

wasted gas. To determine the amount of gas used per hour, the total amount drawn from these tanks was divided by the total number of hours of anesthesia reported in the month. The length of anesthesia reported is the actual time that the gases are flowing.

The most striking figure of these tables is the drop in the amount of nitrous oxid used per hour from 361 to 161 gallons. This and the corresponding drop in the oxygen figures were caused by two factors developed and installed between the two series. The first was the attachment of meters measuring the gas going to each machine so that the anesthetists could note the comparative amount of gas used in any period. Our gas man repeatedly made minute readings during the anesthetics given by our three anesthetists, until we could recognize the anethetist from a chart of these readings. We demonstrated the fallacies of the rate of flow dials on the machines, and the inaccuracy of the meter readings themselves on account of the variations in the pressure. The result of this work was a clear understanding by the anesthetists of when and how they wasted gas. The wasting became less. Our meters were secured with difficulty and at considerable expense, because the high pressure required special construction. But since then one firm, at least, has put suitable meters for this use on the market, and makes a gas machine with meters as an integral part. The second fact was the lowering of the pressure in the pipes leading to the gas machines from 35 to 5 pounds. This pressure is, or should be, reduced by the machines to practically atmospheric pressure. One of the makes of machines that we use handled the lower pressure equally well, but the other did not until we enlarged the ports. It was soon noted that the lower pressure was much easier for the patient as well as more economical. The anesthetist can turn on all the gas the patient can breathe without developing tendency toward possitive pressure in the lungs. Expiration can take place against the gas flow, checking it without effort, and there is always a sufficient volume of gas available for rapid inspiration without developing a negative pressure and effort. The gas flows freely in inspiration, but is automatically checked in expiration.

TABLE I.—AMOUNT OF GASES USED, FIRST SERIES.

	No. Gallons N_2O from Plant	Cost of N_2O from Plant	Cost of N_2O per 100 gallons	Totals gallons N_2O Used	Av. No. Gal. N_2O Used per Hour	Av. No. Gal. O_2 Used per Hour	No. Hours of Anesthesia	Cost per Hour for Anesthesia
Oct., 1913	54,346	$320.02	$0.59	69,646*	470	170	148	$6.18
Nov., 1913	44,601	262.30	.58	61,401*	464	170	132:10	6.63
Dec., 1913	43,296	306.95	.70	44,596*	398	139	112:6	6.70
Jan., 1914	61,176	328.08	.53	62,376*	243	43	256	3.05
Feb., 1914	35,478	243.60	.68	36,178*	262	88	138:44	4.80
Mar., 1914	52,152	296.33	.56	59,652*	326	56	182:59	4.38
Average	48,508	$292.88	$0.61	55,642	361	111	161:42	$5.30

*Small cylinders purchased in this period.

The increase in the cost of manufacture in the second series is due entirely to the lesser amount made and the constant overhead expense for the salary of the man who runs the plant and for other fixed charges. No items of interest or depreciation, but all repairs and replacements are included. In each series, the cost of ammonium nitrate was the same. The recent sharp rise in the price of the nitrate is caused by the increase in the cost of nitric acid due to the war.

ADVANTAGES.

The advantages of this anesthetic which the patient most highly appreciates are the facts that the gases are not disagreeable or irritat-

ing, and that consciousness is lost so promptly. To the patient the starting of the anesthetic is the beginning of the operation, and the sooner consciousness is lost, the better for many reasons. Crile has found that it protects the brain cells from shock more than other anesthetics: especially so, if combined with a little morphin. Following the operation, the patient is not called on to endure patiently discomfort from the irritation of ether in the eyes, throat and bronchial tubes, or on the skin. There are some to whom a greater advantage seems to be the fact that they are not likely to talk or act foolish when coming out from the anesthesia.

In the operating room, gas has an advantage over ether anesthesia because the patient gets under its influence more quickly, saving time and because at the close of the operation the patient is conscious and can be returned to his room as easily as any conscious patient. The familiar scenes of delirium in the second stage of ether, with orderlies holding the struggling patient on the table and the surgeon trying to boss the job and at the same time keep sterile, are entirely eliminated. The ether patient who starts vomiting in the corridor on the way back to his room or ward made more trouble than we realized. Every one took the distressing scene as an occasional necessity, but it certainly never made it any easier for others to face the ordeal of an operation.

The advantages of nitrous oxid anesthesia are best appreciated in the wards, and it is here that the hospital gets back some of the initial cost. It costs a hospital money to care properly for a noisy vomiting ether case in a side room, not only in the nurses' time devoted to the case, but in the effect on the other patients. Comfortable ward patients are as curious as children, and the full details of the ether room scenes never fail to reach the newest patient, creating in him added apprehension and dread. It costs money to have house doctors and head nurses busy explaining away the apprehensions and dread of an operation, and to keep the courage up even after the surgeon has convinced as to the necessity and comparative safety of the impending operation. The return of a patient to his ward bed conscious and comfortable directly from the operating room gives a very different impression as to an operation from that given by a return after a day or so spent in the side rooms. Every patient knows that side rooms are for things the others must not see. It costs money to keep a private room patient convinced that water is withheld for his own good, and convinced kindly and tactfully enough to dispel the suspicion that it is but a rule and red tape that should not apply in his case.

With pure gases, vomiting is extremely rare; when morphin is used it comes about as must be expected from the use of this drug independent of anesthesia, and it resembles morphin vomiting in type. Pneumonia is apparently much less frequent with nitrous oxid, and the same is true of postoperative shock; but the cause of either of these in any given case is so obscure that it is hard to fix the re-

TABLE 2.—AMOUNT OF GASES USED, SECOND SERIES.

	No. Gallons N_2O Made	Cost of N_2O	Cost per 100 Gal.	Av. No. Gal. N_2O Used per Hour	Av. No. Gal. O_2 Used per Hour	No. Hours of Anesthesia	Cost per Hour for Anesthesia
Nov., 1914	27,192	$216.85	$0.79	153	85	177:20	$3.97
Dec., 1914	31,002	221.20	.71	172	53	180:17	3.46
Jan., 1915	18,424	123.52	.67	153	62	119:26	4.71
Feb., 1915	18,582	129.52	.69	166	107	111:39	4.81
Mar., 1915	25,962	169.60	.65	158	54	163:44	3.41
Apr., 1915	26,071	175.40	.67	162	60	160:43	3.75
Average	24,539	$172.68	$0.70	161	70	152:12	$4.02

sponsibility. Since we began the use of nitrous oxid, there have been many other changes and improvements in the care given our patients which should have an effect on the pneumonia and surgical shock percentages. We are certainly getting much less postoperative shock and pneumonia than formerly, and nitrous oxid has undoubtedly contributed largely to this change.

Many patients, especially minor operative patients, are able to leave the ward much sooner. Not only is the day in the ether room lost, but it often requires another one in the ward to bring back the expended energy. The cost of many extra days' treatment saved can properly be credited against the gas anesthesia bill.

TABLE I.—DETAIL OF THE COST PER HOUR.

	First Series	Second Series
Nitrous oxid	$2.20	$1.12
Oxygen	.25	.16
Anesthetists	2.45	2.50
Incidental items, repairs, etc.	.40	.40
Total	$5.30	$4.18

ADMINISTRATION.

Under the administration of nitrous oxid, this paper can mention only a few observations of a skeptical hospital administrator who has watched the development of skill in its use, More than half of nitrous oxid anesthesia was once carbon dioxid asphyxia; blue-black patients were the rule. Now we know that cyanosis at any stage of the anesthetic is evidence either of poisons in the gas or of faulty, incompetent administration. It is not necessary, and is always harmful. Enough oxygen should be given at all times to preserve normal color, but more is a waste. Perfectly normal color can be maintained while the patient is presenting all the symptoms of asphyxia, including convulsions. For this reason rebreathing to any extent is dangerous, and is not justified by the gas saved. Without the color to guide, the percentage of carbon dioxid in the alveolar air may mount unnoticed to levels dangerous through its effect on the brain centers.

The lesser degree of muscular relaxation in nitrous oxid anesthesia is sometimes annoying to the surgeon. It can be overcome by the mixing of a little ether vapor when the relaxation is needed, and all machines are equipped to do this. The results in the matter of losing the advantages of nitrous oxid anesthesia are in exact proportion to the amount of ether used.

Proper appreciation of nitrous oxid as an anesthetic and an analgesic has been delayed by the fact that it could be used by the unskilled without horrible results traceable directly to the lack of skill, and by the fact that it was mentally classed by anesthetists with ether, chloroform and ethyl chlorid as an anesthetic, and its effect expected to correspond with that class. Temporary harmless conscious analgesia for dentistry, childbirth and other minor surgery may seem too good to be true, but it is at hand. Analgesia and unconsciousness without a profound or lasting impression on the central nervous system is the ideal for major surgery. Nitrous oxid in skilled hands can produce both, in unskilled hands, neither.

EVERY INDIVIDUAL IS A COSMOS IN HIMSELF AND DEMANDS A PAINSTAKING SELECTION AND MODIFICATION OF THE ANESTHETIC MEANS PARTICULARLY SUITABLE TO HIS, AND ONLY TO HIS, CASE. PERSONAL, PHYSICAL, EMOTIONAL, TRADITIONAL, ENVIRONMENTAL, RACIAL, CLIMATIC AND MANY OTHER FACTORS AND THEIR PARTICULAR MIXTURE IN EACH PATIENT DETERMINE THE SELECTION OF THE ANESTHETIC METHOD OF CHOICE OR ITS MODIFICATION TO MEET INDIVIDUAL REQUIREMENTS.

—*Rich. H. Riethmüller.*

ETHER-OIL COLONIC ANESTHESIA . HISTORICAL EVOLUTION OF RECTAL ANESTHESIA . THE ANIMAL RESEARCHES OF WALLACE . RATE OF EVAPORATION OF ETHER-OIL MIXTURES . INVESTIGATIONS OF BASKERVILLE . NOBLE'S EXPERIMENTS ON THE BACTERICIDAL ACTION OF ETHER-OIL MIXTURES . EARLY CLINICAL RESULTS AND CASE REPORTS . ANALGESIA . PHYSIO-PATHOLOGY . TECHNIC OF ADMINISTRATION . AUTHOR'S, LUMBARD'S AND LATHROP'S . INDICATIONS, CONTRAINDICATIONS AND ADVANTAGES.

BY JAMES TAYLOE GWATHMEY, M. D., NEW YORK CITY, N. Y.

SINCE THE INTRODUCTION of Ethel-Oil Colonic Anesthesia, it has received the endorsement, not only of expert anesthetists, but also of discriminating surgeons and specialists, and has, in a comparatively short space of time, established itself as one of the routinely efficient, safe and satisfactory methods of anesthesia. The extended use to which the technic is being subjected makes it advisable to enter into a detailed consideration of its evolution, its basic principles, its accomplishments and possibilities.

SOME HISTORICAL CONSIDERATIONS ON THE EVOLUTION OF RECTAL ANESTHESIA.

The fact that the intestinal mucosa is especially efficient in transmitting gases to and fro from the blood, prompted the first colonic administration of ether. To quote from Sutton:

"As early as 1808, Erman,[1] opened the abdomen of *cobitus fossilis* and observed that when air was swallowed the liver and the intestinal veins of the fish became bright red; while when hydrogen or nitrogen was submitted the color of the organs changed to dark purple. Baumert,[2] in 1855, analyzed the gas passed per rectum by the same kind of fish and found a marked decrease in the oxygen content and a corresponding increase in nitrogen when swallowing of air had been prevented for several hours. Jobert,[3] in 1877, discovered that in *callichthys asper*, a Brazilian fish, air swallowing is essential to life, the fish dying in about 2 hours if prevented from the exercise of this accessory respiration. In mammals, also, similar phenomena have long been known. Thus Paul Bert,[4] in 1870, found that if the trachea of a kitten be clamped, the animal will die in about 13 minutes, but, if the intestines be inflated with air, at the same time, life may be prolonged for 21 minutes. A similar absorption of oxygen by the intestinal circulation in man is indicated by the results of Tappeiner,[5] who in 1886, on analysis of gases from various portions of the alimentary tract of an executed criminal, found in the stomach 9.19 per cent. of oxygen, in the ileum only a trace and in the colon and rectum none at all, while the percentage of carbon dioxid showed a regular increase from stomach to colon."[2a]

Roux[6] seems to have been the first to suggest colonic ether anesthesia. In the same year, 1847, Pirogoff,[7] in a volume on etherization, published in St. Petersburg, reported his use of liquid ether mixed with water, injected per rectum, with a view of facilitating the performance of operations on the head and neck. This method was tried by others, notably y'Yhedo[8] and Duprey,[9] who, by employing injections of liquid ether, pure or diluted with water, produced complete anesthesia, Magendie, called attention to the dangers of this method, and ether vapor was substituted for the liquid, with markedly better results. Although Pirogoff, reporting eighty-one cases with two deaths, wrote enthusiastically concerning it, the rectal method did not gain in adherents, and no mention of its use appears again in medical and surgical literature until thirty-seven years later.

In 1884, it was revived with favorable results by Yversen of Copenhagen and Mollière[10] of Lyons, who introduced a new technic by using a Richardson's hand-bellows for

forcing the vapor into the rectum and later an india-rubber tube connected with an ether container immersed in water at 122° F. The vapor was generated by heat and forced into the rectum gradually by the pressure incident to its generation. Usually not more than two ounces of ether was used. In five or ten minutes the patient could taste the ether and became drowsy. This procedure was supplemented by inhalation.

In the same year, in this country, Weir[11] recorded, in the *Medical Record,* the case of an infant in which rectal etherization had proved fatal, death resulting from melena within twenty-four hours after an operation for harelip. Bull[12] also reported adverse results in seventeen cases in which the complications were melena, diarrhœa and even profound stupor and asphyxial symptoms. The cases of many other physicians were also published, among them those of Harter, Wanscher[13] and Post,[14] all of whom reported grave after-effects. Bloody diarrhœa often accompanied the procedure, although it was demonstrated again that complete narcosis could be produced. These objections—bloody stools, rectal irritation, believed to be due to the effect of pure or diluted ether upon the mucous membrane of the gut, inability to control the stages of narcosis and to measure the amount of ether vapor passing into the rectum, caused the second failure of the rectal method to gain serious recognition.

CUNNINGHAM'S METHOD OF RECTAL ANESTHESIA.

It was not until 1902 that the first great advance was made in colonic anesthesia. In that year, while rectal feeding as advocated by Ochsner of Chicago was being used in many cases at the Boston City Hospital, Cunningham devised an apparatus which would permit of the introduction of ether-laden air only and in collaboration with Post, it was used in the Boston City Hospital without the complications which so frequently occurred with the old method. It was tried by others and pronounced practicable. However, Cunningham did note *"colicky pains and painful distention"* as after-effects in some cases and *in all cases he was forced to start anesthesia by inhalation.* In 1903 and 1904, Dumont[15] published case-records of anesthetization by this method without unfavorable symptoms, and Krugeline,[16] in 1904, wrote of 43 rectal anesthesias which had also proved successful.

In 1905, Cunningham and Lahey,[17] in the *Boston Medical and Surgical Journal,* published their first report on 41 cases in which there were no deaths, and no diarrhœa or bloody stools. Stucky[18] commended the method in the *Journal of the American Medical Association,* in 1906, in a report of 4 cases and in the same year, Lumbard[19] used rectal narcosis in performing four laparotomies. These demonstrations of the practicality of the Cunningham technic lent new impetus to the adoption of rectal etherization by many surgeons and anesthetists.

Buxton[20] also used this method pretty extensively, with the addition of an interceptor to prevent the passage of the liquid ether into the gut, and found that it *"answered admirably for operations about the mouth, nose and post-buccal cavities, for staphylorrhaphy, and for operations for the relief of empyema."* In the 1907 edition of his famous work *Anaesthetics,* he stated that for the removal of the tongue, for excision of the jaw, or jaws, and for plastic operations about the face, he had found that the method gave greater facilities and freedom to the operator than any other plan he had tried but also reported that he had met with grave complications, *"which, although in part due to the physical condition of the patients, were undoubtedly not wholly independent of irritation caused in the intestines by the entrance of the ether vapor."* In discussing the after-effects, he said: *"Colicky pains in the intestines, urgent tenesmus, diarrhoea sometimes dysenteric in character, painful distention of the intestinal tract with more or less severe collapse, are complications which have been recorded. Deaths have occurred."*

In 1907, Leggett[21] perfected the Cunningham apparatus by the addition of an exhaust tube connected with the vapor tube for the relief of intraintestinal pressure and evinced his satisfaction with the method in a report on several animal experiments, as well as 31 personally conducted cases which showed incomplete anesthesia in three cases, bloody stools in one case and no fatalities.

Again, in 1908, Dumont published his experiences with rectal etherization for which he used a modified form of the apparatus of Buxton, with the maintenance of smooth narcosis and almost no postoperative complications. Yet he advised against its use in any but exceptional cases without intestinal lesions, under the supervision of an expert anesthetist. In 1908, also, 68 head and neck cases were reported from the clinic of Professor A. Kadhan[22] at St. Petersburg, in 61 of which narcosis was smooth, in five incomplete and in two a failure. Induction was by inhalation; maintenance of the anesthesia, by the rectal method, the duration varying from ten minutes to two hours and forty-five minutes. The report further stated that an average of 1.2 grams of ether was used per minute for both the induction and maintenance of anesthesia but during the rectal administration the average fell to 0.6 gram. Awakening was prompt with bloody diarrhœa in one case, blood-streaked stools in five, abdominal pain in three and vomiting during anesthesia in three.

In the following year, Denny and Robinson[23] announced their success in a series of ten cases and Baum[24] wrote of eight in which three proved entirely satisfactory; two were restless and one, epigastric hernia, was dangerous on account of distention; in two there were prolonged abdominal pain on induction and marked distention, in one of which there was profuse postoperative hemorrhage and in the other, a gangrenous and perforated cecum and general peritonitis resulting in death. In the same year eighteen cases were published by Carson,[25] in two of which failure was due to insufficient preparation and in one to bleeding from the rectum. Two extreme cases, an extensive carcinoma of the face and a hyperthyroidism, resulted in death. In anesthetizing a large, delirious man it was necessary to use the mask throughout the operation. In 1909, also, Legueu, Morel and Verliac[26] first used oxygen as the vehicle for the ether-vapor and pronounced the method, when properly conducted, no more dangerous than the pulmonary.

In 1910, there appeared further rectal anesthetic case-reports by Sutton[27] who used a new apparatus and technic in about 140 cases at the Roosevelt Hospital; another very comprehensive paper by Cunningham;[28] a new apparatus by Thomas[29] for rectal and pharyngeal anesthesia almost identical with that of Sutton; 47 cases by Churchill,[30] using the apparatus of Leggett, and 11 cases by Sanders[31] with a slight modification of Sutton's apparatus in the addition of a chloroform vapor generator to meet the need for accessory inhalation. Of the forty-seven cases anesthetized by Churchill, with ages ranging from six months to seventy-three years, all but seven were satisfactory. Lessening of postanesthetic nausea and vomiting was noted. Alcoholic subjects were more easily anesthetized than by inhalation, which is true also of the ether-oil method.

SUTTON'S METHOD OF RECTAL ANESTHESIA.

The most marked advanced in anesthesia by colonic absorption was that made by Sutton,[28] who used the original apparatus of Cunningham plus the branch tube for exhausting the contents of the gut introduced by Leggett as a basis for his new apparatus. Sutton's apparatus consists of a generator in which the mixture of oxygen and ether is produced, an afferent tube system which carries this mixture into the intestine, an afferent tube system for the purpose of exhausting the contents of the gut and a safety-valve water manometer that automatically blows off at a pressure of twenty millimeters. Sutton reports 140 etherizations with this apparatus, with careful records of the first 100 in the surgical service of George E. Brewer, of Roosevelt Hospital. The other forty were private cases all of which proved satisfactory. *"In only one case was an attempt made to administer the anesthetic per rectum from the beginning. This proved so slow, and was so uncomfortable and distasteful to the patient, that, after about twenty minutes, a cone was used to complete the initial establishment of the anesthesia. Inasmuch as there is no real indication for beginning the administration by rectum, the writer (Sutton) has never made a second attempt to do so."* In the 100 cases the ages ranged from 2 to 77 years. The longest operations of the series took 2 hours and 20 minutes; the shortest, 5 minutes. The average consumption of ether was 87 grams per hour. 12 of the 100

cases had preliminary injection of morphin and scopolamin and 43 supplementary administrations by inhalation of chloroform. Eructation of gas followed in 12 cases, only 4 of which occurred out of 71 cases in which a maximum pressure of 20 millimeters in the bowel was adopted. There was slight perspiration in 18 cases and postoperative vomiting in 43, but of these several felt no nausea. 12 suffered abdominal pain. In 5 there were bloody stools or blood-streaked returns from the postoperative enemata but without noticeable weakness or abdominal pain. In the most severe case of all there was persistent vomiting and continued passage of small quantities of blood for three days. All cleared up in the course of a few hours to three days (Sutton). In this series of cases there were 5 deaths, none of which the operating surgeon considered might be attributed to the method of administration. One other death occurred in Roosevelt Hospital, where this method was used on a five-year-old child during a staphylorrhaphy lasting fifty minutes .

Summarizing his discussion of cases Sutton states:

"This method, safeguarded by such improved apparatus as that described, and by the use of oxygen as a vehicle for the ether vapor, is one of extreme safety in the absence of definite intestinal lesions ..... The colonic method of administration of ether is more complex than the pulmonary method in general, and requires from the anesthetist a broader appreciation of the physiological factors involved. For these reasons alone its field of usefulness is limited to cases in which it presents distinct advantage over the pulmonary method. It is, therefore, not a method adapted to the experimental use of the tyro, but rather a valuable addition to the armamentarium of the trained anesthetist.... The only point against the method in cases where its employment is indicated is the occasional difficulty in maintaining profound anesthesia without the use of the supplementary mouth tube."

Although good results were obtained by Sutton under the guidance and supervision of Brewer, the operating surgeon, who was also enthusiastic about the method, others were less successful and the procedure again lapsed into disuse. There was no special reason for abandoning this form of ether-vapor rectal anesthesia except that an extensive and somewhat complicated apparatus was required.

In the 1912 edition of *Anesthetics and Their Administration* Hewitt[32] says: *"If the risk of diarrhoea, melena and after-stupor could in any way be greatly reduced rectal etherization would be strongly indicated in certain cases." It has now been demonstrated that the latest form of rectal anesthesia—ether-oil colonic anesthesia—does more than simply greatly reduce these distressing after-effects. It has done away with them completely.*

ANIMAL EXPERIMENTATION IN THE DEVELOPMENT OF ETHER-OIL COLONIC ANESTHESIA.

In studying the anesthetic value and technic of ether introduced in solution per rectum, experimental laboratory work was conducted under the immediate supervision of Professor Wallace of the Pharmacological Department of the University and Bellevue Hospital Medical College. Although between 20 and 30 dogs were experimented upon, in only one instance did death occur as the result of the anesthetic and in that case, intentionally. In several cases, before the dosage was determined, the animals were rescued from the danger zone by simply washing out the rectum. Autopsies were performed at irregular intervals upon others, and no contraindications to the method were found. The small, short rectum of the dog proved a great hindrance to experimentation, but we persisted until perfect anesthesia was obtained in several consecutive cases. The following method was generally employed:

Several hours before the administration of the solution, a saline cathartic was given by a stomach tube; half an hour before, a subcutaneous injection of morphin sulphate, from 0.01 to 0.03 grams; and immediately before, a cleansing enema of soap and water. The animal was then placed on its back on a holder, and a fairly stiff rubber catheter inserted into the rectum and pushed up the colon for about 10 inches. The ether solution was placed in a bottle having an outflow tube at the bottom attached with rubber tubing to the catheter. The bottle was then raised to any desired height, from one to six feet, and the flow regulated by a screw clamp on the tubing.

In the first experiment performed, a 5 per cent. ether solution in normal saline was used. About 500 c.c. of this solution was slowly injected into the colon. A very mild excitement stage ensued, and complete anesthesia continued for thirty minutes, followed by gradual recovery. There was a watery discharge from the rectum during the recovery stage, but no diarrhœa on the following day. The experiment was repeated on a second dog, under the same conditions, but complete anesthesia was not obtained. The concentration of ether in the aqueous solution proved so small that excessive volumes of liquid were required, and the ether parted from the solution so very rapidly that experimentation with it had to be abandoned.

I next suggested combining the ether with oil. Since ether is miscible in all proportions in oil, it was hoped, by using a stronger solution of ether than would be possible with any known aqueous solution, to reduce the total bulk of the fluid induced into the colon.

Experiments in the laboratory of the College of the City of New York, under the supervision of Professor Charles Baskerville, were then conducted to ascertain the difference, if any, in the time required for the separation of ether from various oils, and it was found that, regardless of whether the oil was animal, vegetable or mineral, or whether a 25, 50 or 75 per cent. mixture was used, the rate of evaporation remained constant. (*See*: Experimentation on the Rate of Evaporation of Ether from Oils).

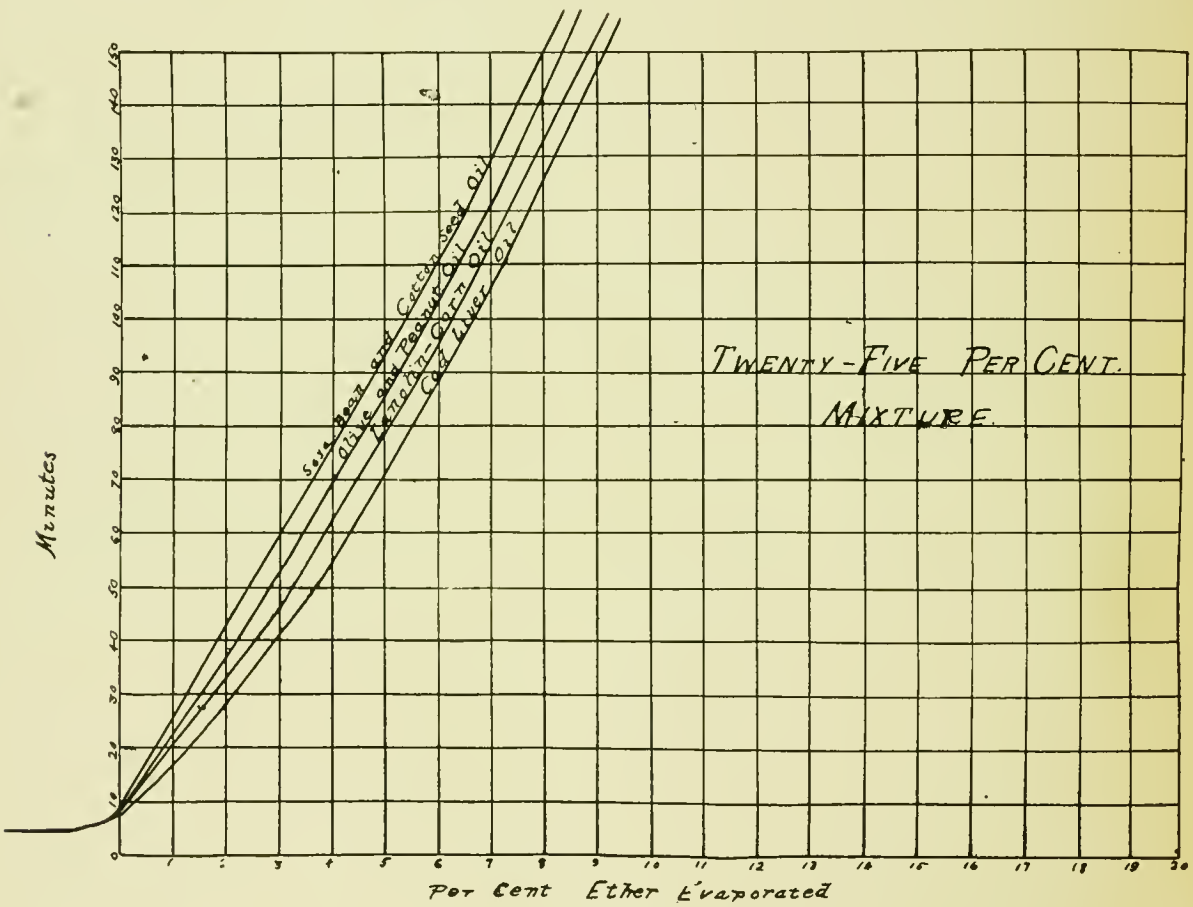


CHART I.

The experimental procedure with animals was then changed, in that the ether was given dissolved in oils and in greater concentration. In one experiment in which 100 c.c. of ether in 250 c.c. of olive oil, a 40 per cent. solution, was injected into a dog of 10 kilograms, the animal became completely narcotized in one hour, when the whole solution had been injected. The anesthesia persisted with a good pulse and regular, deep breathing for 45 minutes. Then breathing became short and irregular; respiration gradually became weaker and stopped fifteen minutes later, death resulting. No effort whatever was made to save the animal. This dog had received a large amount of morphin preliminary to ether injection.

In 2 other experiments in which no morphin was given, one dog, weighing 6 kilograms, received 150 c.c. of a 40 per cent. ether solution, and one, weighing 6 kilograms, 190 c.c. of a 40 per cent. solution. In neither case was complete anesthesia obtained. In the remaining experiments a 55 to 75 per cent. solution was given, the amount of ether injected being from fifty to seventy-five cubic centimeters. Ten successful experiments were carried out, with complete anesthesia and no alarming symptoms.

The shortest time required for surgical an-

esthesia was 5 minutes; the longest, 50. The duration of anesthesia after the ether injection was stopped averaged about an hour, except in cases in which the colon was washed out, when recovery set in promptly. In no case was there any evidence of more than a mild irritation of the rectum following the ether injection, and this, when present, passed off within twenty-four hours. A flushing of the colon with a large amount of fluid shortened the duration of anesthesia, and the subsequent injection of oil prevented or lessened rectal irritation. The accompanying experiment is representative.

EXPERIMENT.—Dog; weight, 12 kg.

10:30 A. M.: Administration by stomach of 10 gm. magnesium sulphate in 100 c.c. water
3:20 P. M.: Subcutaneous injection of 0.02 gm. morphin sulphate.
3:30 P. M.: Rectum washed out.
3:45 P. M.: Injection of 125 c.c. ether solution (75 per cent. in cottonseed oil) into colon at a pressure of 20 m.m. Hg.
4:01 P. M.: Anesthesia complete with no preliminary excitement stage.
4:05 P. M.: Rectum washed with water.
4:10 P. M.: Recovery beginning.
5:00 P. M.: Animal able to run about.

Slight diarrhœa during night and the following day.

EXPERIMENTATION ON THE RATE OF EVAPORATION OF ETHER FROM OILS.

Professor Charles E. Baskerville's investigations in the laboratories of the College of the City of New York in demonstrating the constancy in rate of evaporation of ether from oil, which is a most important factor to be considered in ether-oil colonic anesthesia, are invaluable in placing this method upon a firm scientific basis. A comparison was made of the rate of evaporation of ether from different mixtures of ether and the same oil, a comparison of the rate of evaporation of ether from the same per cent. mixtures of different oils

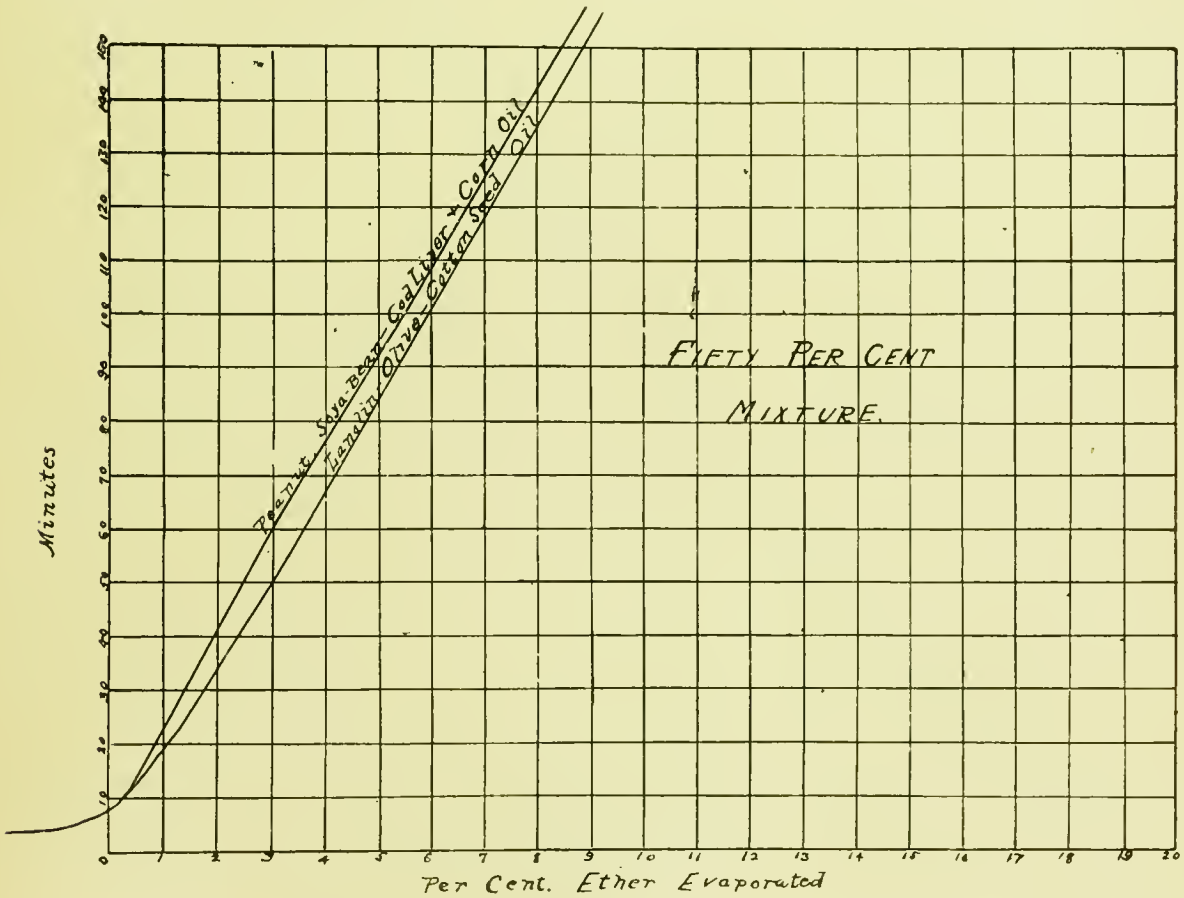


CHART II.

and ether and the influence of surface on the rate of evaporation was also determined. To quote from Dr. Baskerville's report (2) in the *Proceedings of the American Philosophical Society*, August, 1915:

"As the result of much preliminary experimentation, the following mode of procedure was settled upon. Large glass tubes were calibrated to 1 cc. from 20 c.c. to 105 c.c. The mixtures of 25, 50 and 75 per cent. of oil and ether were carefully placed in the tubes.

"Since the evaporation of any liquid depends upon the partial pressure of that liquid at its surface, the higher the glass wall above the surface of the ether-oil mixture, the heavier the column of ether vapor resting on the surface of the mixture, the slower will be the evaporation, consequently the different oil mixtures with the different percentages of ether were experimented with in the same tube filled to the same height in each experiment.

"In the experiments to determine the influence extent of surface played upon the rate of evaporation, the same precautions were taken as to height of walls of

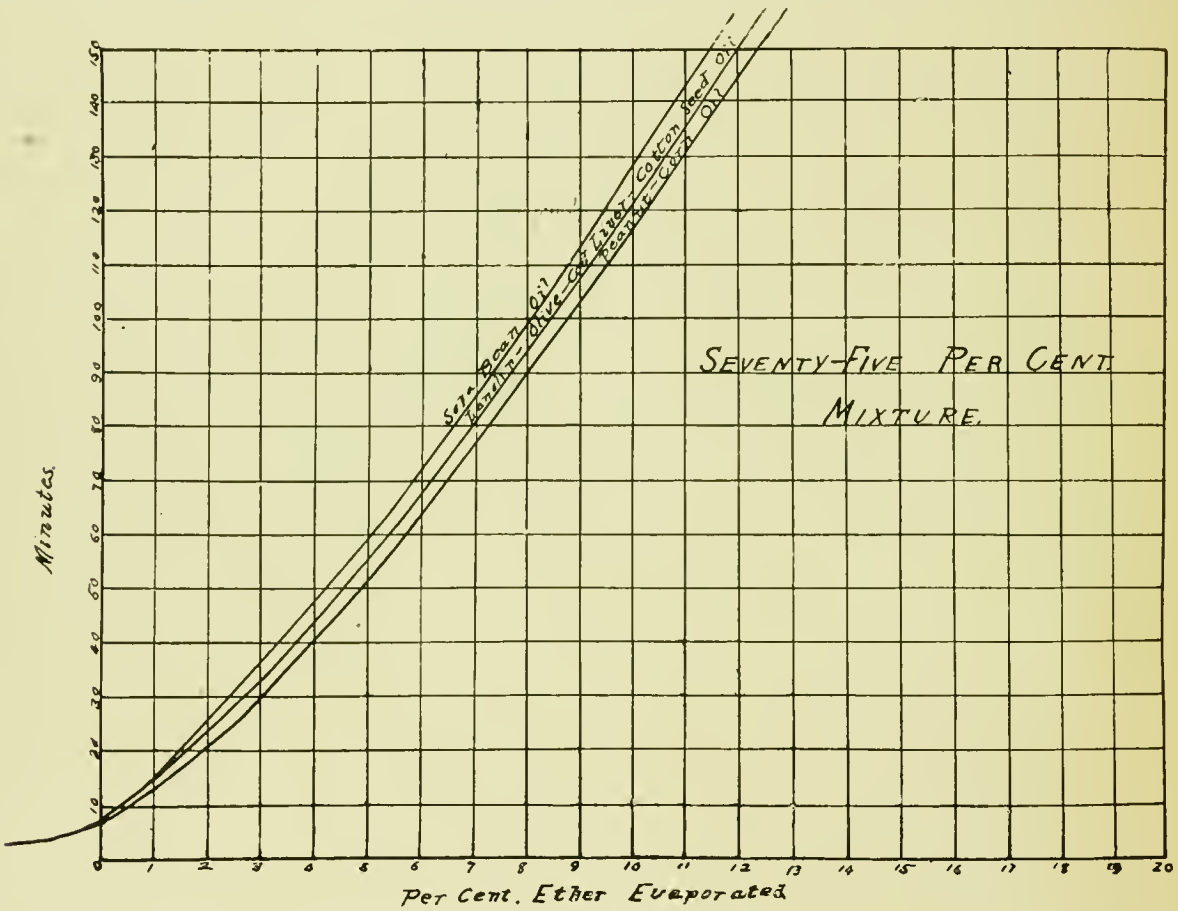


CHART III.

The tubes were weighted with lead and placed in a thermostat, whose temperature was so regulated as not to vary more than +0.03° C. from 37° C., the same being controlled by a toluene + mercury temperature regulator. All connections (gas, water, etc.) were made with lead pipe for safe use over night, as occasion arose. The water in the bath was stirred by a system of paddles and shaft operated through belt and pulleys by a small hot air engine. The tubes were immersed in the bath to within 2 cm. of the tops. During the first five minutes two readings were made in each case to get the highest point to which the volumes expanded upon heating up to 37° C. After that readings were made every 5 minutes for 2 or 3 hours.

the containing vessels. In the largest areas worked with, this involved using as much as 600 c.c. of the mixture. As the 75 per cent. mixture had been found most satisfactory clinically, this was determined with that mixture only.

"The ether used was that prepared under my supervision and was 97 per cent. absolute with 3 per cent. absolute alcohol, being free from acids, aldehyds and water.

"The oils used were of three types, vegetable, animal and mineral, being respectively, olive, cotton seed, corn, peanut and soya-bean; cod-liver and lanolin (anhydrous); and Russian mineral oil. All the vegetable oils except olive, were refined by a process devised by

the author (Baskerville: Refining Oils, *Oil, Paint and Drug Reporter,* May, 1915). and were neutral. The other oils were purchased in the open market.

"The data obtained for the 25, 50 and 75 per cent. mixtures, vegetable and animal oils, are shown graphically in Charts I, II. and III. In the curves the abscissæ show the percentage of ether evaporated (based on volume measurements) and the ordinates time of the evaporation.

"Chart IV. (Selected at random from charts made for each oil). Shows the difference in rate of evaporation 25, 50 and 75 per cent. mixtures with one oil.

"Chart V. shows the effect of increased surface on the rate of evaporation. One oil only was selected to show the principle, which is: the rate of evaporation bears a direct ratio to the surface exposed

"These experiments were made in glass, hence they do not disclose all the factors in the conduct of such mixtures in contact with the walls of the colon, for there the principles of osmosis and diffusion are involved. But these observations demonstrated several striking facts:

"(1) While ether boils at 34.6° C., it does not escape violently from an ether-oil mixture, as from an aqueous mixture when the mixture is heated higher, namely, to the body temperature of 37° C.

"(2) The *rate* of separation of ether from the oil quickly acquires a definite and fairly fixed speed.

"The significance of this conduct cannot fail to be of great importance, for by this means the proper content of ether may be maintained in the blood to produce any desired physiological effect that has a quantitative relation thereto, for example, the third or surgical stage of anesthesia."

Thus, it was demonstrated that, regardless of whether the oil was animal, vegetable or mineral, that is, corn, cotton-seed, peanut, cod-

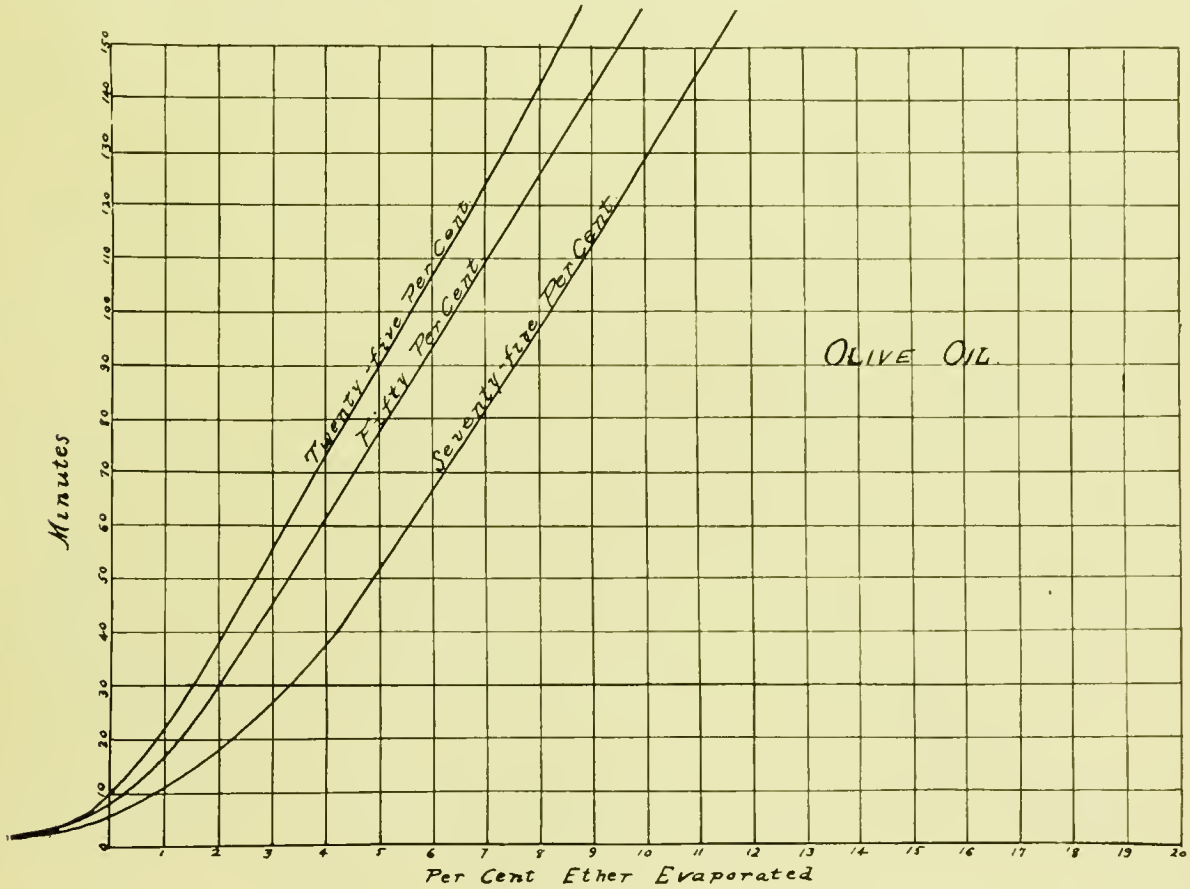
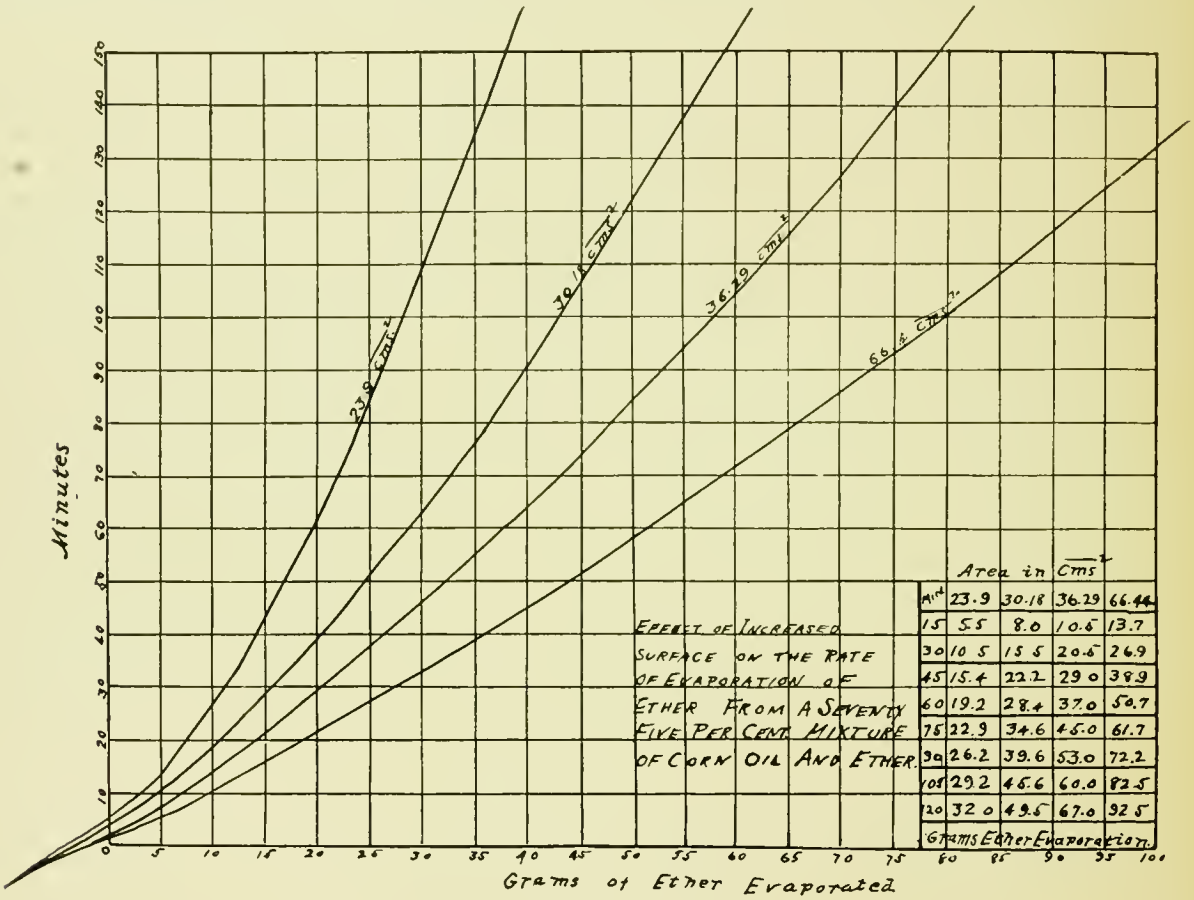


CHART IV.

liver, lanolin, soya-bean or olive oil, or whether a 20, 50 or 75 per cent. mixture was used, the rate of evaporation remained constant. Furthermore, if the mixture was placed in a vessel with greater surface area than that of a test-tube, the evaporation was still constant, although the rate was increased.

These charts, showing the percentage of ether evaporation during a period of two and

one-half hours would convince the most skeptical that, in as far as this factor is concerned, giving ether-oil colonically is a safe procedure admitting of an absolutely even plane of anesthesia, which would not be the case if the ether evaporated irregularly either in point of time or quantity. The charts show, furthermore, that the patient does not absorb a tremendous amount of ether immediately upon injection, which would result in anesthetic shock, but that he becomes anesthetized gradually in accordance with the constancy in evaporation of the ether from the mixture in the colon.


Minutes
Grams of Ether Evaporated
23.9 Cms²
30.18 Cms²
36.29 Cms²
66.4 Cms²
Effect of Increased Surface on the Rate of Evaporation of Ether From A Seventy Five Per Cent. Mixture of Corn Oil And Ether.
Area in Cms²
Grams Ether Evaporation.

Min	23.9	30.18	36.29	66.44
15	5.5	8.0	10.6	13.7
30	10.5	15.5	20.6	26.9
45	15.4	22.2	29.0	38.9
60	19.2	28.4	37.0	50.7
75	22.9	34.6	45.0	61.7
90	26.2	39.6	53.0	72.2
105	29.2	45.6	60.0	82.5
120	32.0	49.5	67.0	92.5

CHART V.

EXPERIMENTS ON THE BACTERICIDAL ACTION OF ETHER-OIL MIXTURES.

In the Laboratories of the Department of Health of New York city experiments were conducted under the supervision of the Director of the Bureau, William H. Park, Dr. Cary W. Noble doing the detail work, on the bactericidal action of ether-oil mixtures, using 5, 10, 20, and 30 per cent. mixtures against the B. Coli. These tests showed that 10, 15 and 20 per cent. ether-oil mixtures killed practically all B. Colin 2½ minutes exposure, in tubes of broth.

Since infection from the colon bacillus is a factor to be reckoned with in many surgical operations, it may be inferred from these tests that the bactericidal action of the ether-oil mixtures affords an added element of safety with this method of rectal anesthesia.

During 1911 to 1914, Dr. H. C. Coe reported 34 cases of colon bacillus infection in his service at Bellevue Hospital.[8] As shown in

Chart vi., the oil itself has an apparently inhibiting but probably no bactericidal effect.

Agar tubes were inoculated at the same time that the broth tubes were. These were

CHART VI.

	Minutes					
Time of Exposure	2½	5	7½	10	12½	15
10. cc. oil only O. 2cc. B.Coli	+	+	+	+	+	+
20% Ether-oil, (10cc) O. 2cc. B.Coli.	—	—	—	—	—	—
15% ether-oil	—	—	—	—	—	—
10% ether-oil	—	—	—	—	—	—
5% ether-oil	+	+	+	+	+	+
CONTROL EXPERIMENTS						
10. cc. Salt sol. (0.85%) O. 2cc B.Coli	+	+	+	+	+	+
1-80 carbolic	+	—	—	—	—	—
1-90 carbolic	+	+	—	—	—	—
1-100 carbolic	+	+	+	+	+	+
1-110 carbolic	+	+	+	+	+	+

+ = growth; — = no growth

poured into plates which were incubated for 48 hours at 37°C. The colonies which developed are recorded in Chart vii.

It is interesting to note that ether-oil mixtures have a very great bactericidal power. mixtures against a standard typhoid culture. The results are tabulated in Chart viii.

These tests show that the 5 per cent. ether-

CHART VIII.

	Minutes					
Time of Exposure	2½	5	7½	10	12½	15
Olive oil only	+	+	+	+	+	+
30% ether-oil	+	—	—	—	—	—
20% ether-oil	+	—	—	—	—	—
10% ether-oil	+	—	—	—	—	—
5% ether-oil	+	+	+	+	+	+
1-100 carbolic	—	—	—	—	—	—
1-110 carbolic	+	+				

+ = growth, — = no growth.

oil mixtures have an inhibiting effect on typhoid fever bacilli after 15 minutes exposure and that 10, 20 and 30 per cent. mixtures inhibit the growth after 5 minutes exposure.

CLINICAL EXPERIMENTS WITH ETHER-OIL COLONIC ANESTHESIA.

The first successful public clinical demonstration of ether-oil colonic anesthesia was made on September 27th, 1913, at The People's Hospital, New York City, on one of Dr. I. M. Rothenberg's patients, Dr. Rothenberg operating. This work was continued

CHART VII.

	Minutes					
Time of exposure	2½	5	7½	10	12½	15
10. cc. oil only O .2cc B. Coli	430	1900	550	680	820	390
20% ether-oil (10cc.) O 2Cc. B.Coli	10	10	0	0	0	0
15% ether-oil	6	0	0	0	0	0
10% ether-oil	75	42	3	4	1	1
5% ether-oil	65	125	26	31	170	190
CONTROL EXPERIMENTS						
10. cc. Salt sol. O .2cc. B.Coli	21000	25000	25000	25000	25000	25000
1-80 carbolic	2	1	0	0	0	0
1-90 carbolic	190	7	0	0	0	0
1-100 carbolic	1160	190	73	9	5	1
1-110 carbolic	3600	370	170	68	21	14

This would refer especially to surgical cases in the first stage of typhoid fever, although it would be contraindicated in the later stages. It would also have a theoretical bearing upon the use of ether-oil mixtures in other diseases and for other purposes than surgical. Tests were made using 5, 10, 20 and 30% ether-oil with success at Columbus Hospital, at other hospitals in New York City, and in neighboring cities, with its ultimate recognition and introduction into modern surgery as a thoroughly satisfactory method of producing ether narcosis through the rectum.

To keep well within the limits of safety

was the controlling factor in our early hospital work with ether-oil injections, we did not immediately adopt for human beings as large a dosage as had proved successful in our laboratory work with dogs. Consequently the lower percentages of ether proved insufficient for surgical anesthesia in some cases and it was necessary to supplement with ether by inhalation. In the first series patients were given a 40 per cent. ether-oil solution. Results were negative from every point of view. The next series received a 50 per cent. solution. Results in these cases also proved negative, although as much as nine ounces of oil with the same amount of ether were injected at the one time. In the final series from 65 to 75 per cent. solutions were administered, that is, exactly the same percentages that were found effective in animal experimentation and with equally gratifying results. From 200 to 300 cc. of a mixture of three parts of ether to one part of oil was estimated as the correct amount and was used in over 200 successful cases. In half this number, however, it was necessary to supplement the ether-oil anesthesia with an inhalation anesthetic.

At the very beginning of the series, two patients were anesthetized at Roosevelt Hospital in both of whom unpleasant symptoms occurred on the introduction of the solution. In each a supplementary anesthetic was required because induction was attempted with the patient in the dorsal position, which has since been abandoned for the Sims.

EARLY CASE REPORTS OF ETHER-OIL COLONIC ANESTHESIA.

The first report on the experimental work conducted in the development of this method was read by the author before the Seventeenth International Medical Congress in London, August, 1913, and the Lancet, December 20, 1913, contains a discussion of a number of the author's first cases. The ages of the patients ranged from 4 to 71 years.

In all these cases the operations had been witnessed by members of the profession, and in one instance by 40 physicians and surgeons. Careful blood and urine analyses were made before and after operation, and the blood-pressure was taken during operation. Some of the patients were also examined with a proctoscope for possible inflammatory after-effects. None of these examinations showed any contraindications, and patients who had been previously anesthetized by other methods and who were capable of making an intelligent comparison, expressed themselves most enthusiastically in favor of ether-oil. The cases noted are a few of those which are most illustrative of various physiological elements which must be taken into consideration in the colonic administration of ether-oil, and show that judgment must be exercised with regard to the preliminary medication and the amount and percentage of the anesthetic used.

Cases I. to V. indicate the dangers to be avoided and the dosage to be employed.

Case I.—Boy, age, 10 years. Hydrocele and circumcision. Sulphate of morphin, 1-12 grain, was given hypodermically 30 minutes before operation, and also a 5-grain chloretone suppository at the same time; between 75 and 100 c.c. of a 75 per cent. solution were introduced very slowly, the patient falling asleep before the full amount was introduced, sleeping quietly through the operation, and making an uneventful recovery.

Note—In a case of this kind, in accordance with the most up-to-date technic, a 65 per cent. solution would now be used.

Case II.—Girl; age, 9 years. Adenoids and enlarged tonsils. Dosage, 100 c.c. of a 75 per cent. solution without preliminary medication. The child complained slightly as the mixture was injected. The relaxation was perfect, and she left the hospital five hours after operation.

Note—In this case, also a 65 per cent. solution would now be used.

Case III.—Woman; age, 38 years; weight, 125 pounds. Carcinoma of the breast. Operation at the Presbyterian Hospital, New York City, by Dr. Forbes Hawkes. The patient was given 1-6 grain of morphin, and 1-100 grain of atropin hypodermically; 5 grains of chloretone, dissolved in 2 drachms of ether, and mixed with 2 drachms of olive oil, were introduced into the rectum, 30 minutes before operation. Eight ounces of a 75 per cent. mixture were introduced into the rectum in 6 minutes time. The patient was in surgical anesthesia 4 minutes after the total mixture had been introduced. Three ounces were drawn off during the operation as the patient seemed to be too deeply narcotized. The resultant anesthesia was perfect in every respect, the patient breathing quietly as in natural sleep during the entire time of the operation. An uneventful recovery with no nausea or vomiting followed. Blood and urine analyses proved negative.

Note—The fact that the patient did not complain or in any way show that the introduction of the mixture was appreciable is entirely accounted for, in the author's opinion, by the administration of the chloretone. We never give over 6 ounces now. If 8 ounces are given, as soon as deep surgical anesthesia supervenes and *before the operation* begins, 2 ounces should be withdrawn.

Case IV.—Similar to Case III. Operation at the New Rochelle (New York) Hospital by Dr. Cantle.

The patient received 1-4 grain of morphin with 1-100 grain of atropin hypodermically 30 minutes before operation. No suppository was used, and there was slight complaint of discomfort in the rectum as the mixture was introduced. The resultant anesthesia was perfect in every particular. Pulse and respiration were normal, and prompt recovery without any unpleasant after-effects followed. The patient who had been operated upon twice previously under inhalation methods, stated that if she were compelled to undergo another operation, the ether-oil would be the choice of methods.

NOTE—The dosage was not mentioned in this report. The discomfort during introduction of the anesthetic was due, in the author's opinion, to the omission of the suppository.

CASE V.—Woman; age, 37 years; weight, about 150 pounds. Abdominal hernia. Operation at the New York Polyclinic Hospital by Dr. Bodine. The patient was given 1-4 grain of morphin and 1-100 grain of atropin 30 minutes before the operation. At the same time a solution containing 10 grains of chlorctone and 4 drachms of ether with an equal amount of olive oil was introduced into the rectum. Just before operation 8 ounces of a 75 per cent. ether-oil solution were given to the patient in bed. She sank into deep surgical narcosis before the full amount (8 ounces) was introduced. A slight cyanosis indicated an overdose; therefore, 3 1-3 ounces were drawn off, as the patient was placed upon the operating-table. The relaxation in this instance was perfect; pulse and respiration were about normal. The patient slept for 6 hours after completion of the operation and awoke without nausea or vomiting, in a perfectly satisfactory state in every respect.

NOTE—The overdosage in this case would indicate that the correct amount is 6 ounces. At this time we were not using massage over the colon from right to left after operation as a regular procedure, hence the six-hour sleep.

Cases VI. and VII. show that the simplicity of this method does not preclude watchfulness The chief danger lies in the possibility of respiratory arrest.

CASE VI.—Woman; age, 30 years, weight, less than 100 pounds. Pelvic cellulitis. Operation at the Harlem Hospital, New York City, by Dr. Luckett. The patient was given 1-4 grain morphin and 1-100 grain atropin hypodermically, and a suppository containing 20 grains of chloretone as preliminary medication. Eight ounces of a 75 per cent. solution of ether in oil were administered. The patient evidently received an overdose of both preliminary medication and anesthetic. Respiratory arrest occurred a few minutes after she was placed upon the operating-table. Artificial respiration, stretching of the sphincter, and the intravenous introduction of 1,000 c.c. of normal saline were employed. A bag containing a small amount of carbon dioxid was then placed over her face, whereupon respiration recommenced immediately.

During the time of this respiratory arrest, which, according to the operating nurse, lasted 8 minutes, the pulse was full, regular, and approximately normal. The color of the lips and tongue was good. The operation was satisfactorily performed, and the patient was returned to bed. An uneventful recovery is recorded in this instance, with no nausea, vomiting or other ill effects.

CASE VII.—Man; age, 47 years; weight, 160 pounds. Private patient. Excision of the tongue, floor of the mouth, and glands of the neck. Duration of operation, nearly 3 hours on account of the adhesions and abnormalities resulting from a cancerous growth. The patient was given 1-4 grain of morphin with 1-150 grain of atropin hypodermically, half an hour before operation, and 10 grains of chloretone in a suppository at the same time. Eight ounces of a 75 per cent. mixture of oil and ether were administered. The patient dropped to sleep almost immediately. At the end of one hour the pulse was full and regular, but there was stertor which perceptibly increased until respiration ceased for three minutes. The rectum was washed out with cold water, and as much as possible of the mixture was withdrawn. Respiration recommenced without anything else being done, and the operation was continued and completed without further interruption. When the patient was returned to bed the pulse was 72 and the respiration normal. This patient also made an uneventful recovery with no nausea or diarrhœa following.

NOTE—An inhalation anesthetic would have undoubtedly increased the engorgement and congestion usually following such cases. This case is illustrative of the action to be taken in event of overdosage. The rectum should be immediately washed out and one or two ounces of oil injected. Only 6 ounces of a 65 per cent solution should have been used in this case. With this dosage, however, it would have taken the patient fifteen to twenty minutes longer to go under.

Cases VIII. and IX. illustrate the value of this method for insane patients, neurotics and greatly agitated patients.

CASE VIII.—Woman; age, 38 years; weight, 105 pounds. Tumor of the breast. At 9:00 A. M. was given 5 grains of chloretone dissolved in ether and oil; at 9:30 a hypodermic of 1-8 grains of morphin and 1-100 grain of atropin. The patient was insane, and it was necessary that quiet should be maintained and none but the nurse allowed in the room. A 75 per cent. mixture of ether and oil was prepared in an adjoining room, and the nurse was told exactly how to administer the 5 ounces of the mixture required for this case. The nurse carried out the instructions, with no protest whatever from the patient. In 15 minutes the patient was unconscious; she was picked up, and placed upon the operating-table in an adjoining room. The operation was performed with no movement whatever by the patient; lower bowel was siphoned off and thoroughly irrigated; one ounce of olive oil and one pint of cold tap water were left in the bowel. This patient had no nausea or vomiting whatever. She was sufficiently sensible to appreciate that everything possible had been done for her comfort.

NOTE—The possibility of trouble in this case was very great, if the patient learned of the operation. The anesthetic was administered, the operation performed, and the patient returned to bed without ever seeing a doctor.

CASE IX.—Boy, age, 8 years. Broken arm. Operation by Dr. Harold Meeker. Patient greatly agitated. The anesthetic was administered by the child's mother, while he was lying on a sofa, the surgeon being in the next room. There was no preliminary medication or preparation. Patient dropped to sleep quietly, the anesthesia being entirely successful.

Cases X. to XII. are representative of many which confirm the assertion that the ether-oil

method of colonic anesthesia is especially indicated for operation on the obese.

Case X.—Weight of patient, 250 pounds. Umbilical hernia. Operation at the Massachusetts General Hospital. In this case, Dr. Allen, the anesthetist, stated that he dreaded giving the patient any inhalation anesthetic. Relaxation perfect, and anesthesia all that could be desired.

Case XI.—Weight of patient, 240 pounds. Umbilical hernia. Operation at the New York Hospital for Ruptured and Crippled, by Dr. Walker, Dr. Coley and Dr. Gibney being present. Relaxation perfect, and anesthesia all that could be desired.

Case XII.—Private patient; weight, between 200 and 300 pounds. Operation by Dr. Forbes Hawkes. As in all private cases, a nurse preceded the anesthetist, following his directions in regard to administration, his duty being to supplement withdraw, deepen, or lighten the anesthetic according to the indications. The result was ideal.

Cases XIII. to XVI. were borderline cases in which the anesthesia was a problem and required careful judgment as to the amount administered. They illustrate the range of the anesthetists control in making ether-oil colonic anesthesia a safe proceedure.

Case XIII.—Woman; weight, less than 100 pounds. In complete abortion of three weeks standing; pulse 150. Operation at the Mary Gates Hospital, Port Arthur, Texas. As a preliminary 1-8 grain morphin, 1-150 grain atropin, and 10 grains chloretone were employed. Four ounces of a 75 per cent. ether-oil solution were administered. Patient completely anesthetized in 10 minutes, did not vomit, and 3 hours after the operation asked when the doctor was coming to operate. Left hospital four days later.

Case XIV.—Woman; weight, 70 pounds. Panhysterectomy. Operation at the Mary Gates Hospital, Port Arthur, Texas. As a preliminary 1-8 grain morphin, 1-150 grain atropin, and 10 grains chloretone were employed. Four ounces of a 75 per cent. ether-oil solution were administered, and as the patient was not under the influence of the anesthetic in 20 minutes, 2 ounces additional were given. Anesthetization was complete in 5 minutes after this. When brought into the operating-room the patient was too deeply narcotized and 2 ounces were siphoned off. The operation lasted 2 hours and 45 minutes. In recovering from the anesthesia the respirations were unsatisfactory, and the patieut was given 1-2 grain cocain, hypodermically. Patient did not vomit nor ask for water. Recovery uneventful.

Case XV.—Woman; weight 165 pounds. Gallstones. Almost imperceptible pulse. Operation at the Mary Gates Hospital, Port Arthur, Texas. Patient was given a preliminary administration of 1-4 grain morphin, 1-150 grain atropin, and 10 grains chloretone. Eight ounces of a 75 per cent. ether-oil solution were administered. Pulse improved immediately. After establishing ether tension, the patient seemed a little too deeply narcotized, and 3 ounces of the solution were siphoned off before the operation was begun. The anesthesia was supplemented with chloroform when operating on the gall-bladder. Operation lasted 1 hour and 30 minutes. Patient reacted immediately upon irrigation, and made an uneventful recovery, without vomiting.

Case XVI.—Child; age 7 1-2 years; weight, 40 pounds. Septic tonsils; swollen and inflamed glands. Patient an only child, born a *blue* baby. Lips very blue. Operation imperative. Foramen ovale patent; also systolic murmur. Dosage, 2 ounces of a 60 per cent. ether-oil solution, given 20 minutes before operation. It was necessary to complete anesthesia with a few drops of ether on the mask. Duration of operation, 15 minutes. Patient was quite cyanosed during operation. Colon massaged immediately. Residue was drawn off and 2 ounces of olive oil injected per rectum. Consciousness returned in 15 minutes after patient was returned to bed. In this case the solution was given by the nurse. The child did not see the doctors. He went under anesthesia quietly and easily, and came out without nausea or vomiting. He told his mother that he had a nose-bleed while asleep. He left the hospital in three days, and five months later had gained 10 pounds and seemed to be improving.

Note—Any inhalation method would have been contraindicated in this case, especially nitrous oxid and oxygen.

FURTHER CASE REPORTS ON ETHER-OIL COLONIC ANESTHESIA.

Up to July of the year following this report on the first 100 cases of ether--oil anesthesia, the author had employed the method in about 140 cases in the Johns Hopkins Hospital in Baltimore, in the Massachusetts General Hospital, Boston, and in several hospitals in New York City, and had received definite information on almost 500 cases from the following surgeons and hospitals, who had also used it with success: 50 reported by Dr. Heyd of the New York Post-Graduate Hospital; 17 by Dr. Frazier of the New York Post-Graduate Hospital; 20, by Dr. Robinson of the People's Hospital; 37 at Columbus Hospital; 13 by Dr. Schmidt of the Atlantic City Hospital; 29 by Dr. Dye of Erlanger Hospital, Chattanooga, Tennessee; 75 by Dr. Wiltsie of Smith Infirmary; 26 by Dr. Edward M. Foote; 14 by Dr. Meeker; 50 by Dr. Huberet Arrowsmith of the Brooklyn Eye and Ear Hospital; 80 by Dr. Joseph E. Lumbard; 38 by Dr. Cantle; 15 by Dr. R. S. Morton of the New York Polyclinic Hospital; and one case by Dr. John B. Murphy, with the following comments in brief:

Dr. Heyd.—In the 50 reported from the New York Post-Graduate Hospital by Dr. Heyd, eight were supplemented with chloroform. A trace of albumin was found in the urine about as often as when inhalation methods are employed. There did not seem to be an indication to proctoscope any of the patients. In only 3 cases was there postoperative nausea and vomiting. Dr. Heyd concludes: "Where we had plenty of time to give the anesthetic properly, the results have been most satisfactory."

Not included in this list was a private case which also occurred at the Post-Graduate Hospital. The patient was a doctor's wife who had delayed having her tonsils removed for over a year, on account of very great fear of the anesthetic. This new form of anesthesia so appealed to her that she immediately decided upon an operation. The anesthetic was given to her in bed, without any complaint whatsoever, and the operation was entirely successful. However, a hemorrhoidal condition was so irritated by the anesthetic that the patient had to undergo a second operation a few days later for hemorrhoids.

Dr. Robinson.—"The principal case of interest at the People's Hospital was that of a woman weighing about seventy-five pounds, with a temperature of one hundred and four degrees, suffering from general diffuse peritonitis. This patient was held on three and a half ounces of a 75 per cent. mixture for an hour and fifteen minutes. She made an uneventful recovery."

Dr. Wiltsie.—"At the Smith Infirmary, a supplementary anesthetic was required in one-third of the cases. The urine was negative as to pathological findings. Those who had been operated upon previously with an inhalation anesthetic expressed a strong preference for the ether-oil method. Many patients thought they were receiving an ordinary enema, and upon awaking after operation asked when they were to be operated upon."

Dr. Schmidt.—"The elimination of the element of fear is the greatest asset of ether-oil colonic anesthesia. The method was satisfactory in 13 cases coming under my personal observation and there were no bad results following. In only one instance was it necessary to administer a few drops of chloroform to secure greater relaxation of the abdominal musculature. When the indications for its use are more fully understood, this method of Dr. Gwathmey will be more generally used."

Dr. Cantle.—"During the past two months I have supervised the administration of ether-oil colonic anesthesia to 38 children, ranging in age from 2 1-2 to 11 years, for tonsil and adenoid operations. Fear and struggling, so common under inhalation methods, were entirely obviated, as the attending nurse handled the preliminary treatment. In the older children 1-8 grain of morphin was given by mouth one hour before operation and chlorotone, 5 grains by rectum, immediately preceding the ether-oil. Patients became anesthetized in from 10 to 20 minutes. Supplementary etherization was necessary by inhalation in only one instance, and in another case the onset of anesthesia was delayed for 40 minutes owing to poor preparation of the lower bowel."

Five of Dr. Cantle's patients had taken ether before, and all agreed that this was the more comfortable method, the preliminary sensation of choking and suffocation being entirely eliminated and there being no unpleasant after-effects. All patients made good recoveries, with no complications. See also, five of Dr. Cantle's recent cases.

Dr. Foote.—"My general impression of ether-oil rectal anesthesia is so favorable that I shall continue its use."

Dr. Meeker.—In two emergency operations on children by Dr. Meeker no preliminary preparation of any kind was given, yet anesthesia was entirely satisfactory.

Dr. John B. Murphy.—At the time of these reports, July, 1914, Dr. Murphy had used the method but once. He stated that the anesthesia was perfect and that he intended making frequent use of it in his clinic.

Dr. R. S. Morton.—"Speaking as a surgeon, after a trial of ether-oil colonic anesthesia in 15 abdominal sections at the New York Polyclinic Hospital, I am rather optimistic about the method, especially because patients accept this form of anesthesia far more readily than inhalation narcosis, and more especially because they seem to have no recollection of having been operated on, and postoperative complications such as pain, nausea and vomiting are almost entirely obviated. While the obtunding of postoperative pain may be in a measure due to the preliminary administration of morphin and chloretone, I believe that ether-oil colonic anesthesia has a peculiar desensitizing effect on the abdominal viscera, and is also greatly responsible for the pain-free period after operation lasting from four to sixteen hours.

"The integrity of the bowel is in no way affected. None of my cases developed symptoms of irritation of the colon and gas distress presented in only one patient with angulations of the intestines. Respiration, pulse, and temperature, taken before, during and at periods after operation, showed markedly less alterations than under routine methods of inhalation narcosis. Kidney function is not materially affected."

Dr. Arrowsmith.—"Colonic ether-oil anesthesia is really an *epoch-making* discovery in the evolution of narcosis, particularly as applied to the domain of oral, laryngeal and border-line surgery. Laryngological colleagues are finding the method of especial value in bronchoscopic and esophogoscopic cases, where the extraction of foreign bodies is concerned, for the operator may go ahead with his work, uninterruptedly, regardless of the anesthetist and without the annoyance, at critical junctures, of a partial return to consciousness of the patient, which may mean failure of the operative procedure. The method offers a safe, uniform surgical plane of narcosis that persists, with little or no participation on the part of the anesthetist, for two hours. I have employed the technic in cleft palate operations, resections of the jaw and nasal bones, in extensive attacks on the accessory sinuses, laryngostomies and endolaryngeal operations with the suspension laryngoscope. One of my conferes uses it, by preference, for submucous resection of the septum.

"While the skill of Dr. A. F. Erdman made previous methods of rectal ether vaporization satisfactory for operative procedure about the head, face and neck, these older technics cannot compare in efficiency, safety or ease of administration with that developed by Dr. Gwathmey.

Dr. Lumbard.—"A minimal amount of supplementary narcosis may be required in a small proportion of cases. The technic is particularly adapted to stealing *the thyroid*, and is especially valuable in bronchoscopy and operations about the head, neck and chest. The time required for thorough preparation, the prolonged stage of postoperative narcosis, and the contraindication of the method in irritative lesions of the rectum are disadvantages. The technic is available, however, for the extremely nervous and insane. Furthermore, during its conduct there is no tendency to hypersecretion of mucus, and respiration and pulse are more nearly normal than with any inhalation method.

"While not prepared to consider the method foolproof, nevertheless, having tried it on eighty cases for fifteen different surgeons, I am willing to advocate its use in appropriate cases. The Gwathmey method is far superior to all previous methods of colonic anesthesia in its results and freedom from complications." (*See*: Lumbard's Technic).

Dr. Dye.—"After an experience with this method in 29 cases at Erlanger Hospital, Chattanooga, Tenn., I can corroborate the results secured and observed by others."

Dr. J. C. Pate,[26] of Valdosta, Georgia, in an address before the Lowndes County Medical Society in February, 1914, also commended the method and expressed his accord with the author's assertions as to its safety and advantages. He cited the following case in which he used ether-oil to his entire satisfaction:

"G. S., a negro woman, age 25, aborted the night before I was called to see her. Upon arriving at her home, I found her to be suffering from hemorrhage, which had been and was profuse. A currettage was thought best. Patient was given two colon irrigations (high), and at the end of the second irrigation the fluid returned clear. Patient was given hypo of morphia and atropin about thirty minutes before the operation and at the same time I injected two drachms each of ether and olive oil, mixed with chloretone, ten grains. As the patient weighed 120 pounds, I only used six ounces of a 75 per cent. solution of ether in olive oil. I assumed about six minutes to let solution drain into rectum. Within four minutes patient was asleep, with no loss of reflex to lid. Patient seemed to be more asleep from natural resources than anesthetized. Operation was completed in about five minutes and patient straightened in bed. Pulse at this time was 76, and respiration was eighteen per minute. I left word with the family to call me up as soon as patient regained consciousness. In about two hours I received a call and upon reaching the bedside the patient seemed to be of clear mind and memory. She complained of being numb all over, and, as she expressed it, she seemed to be dead from the neck down. This numbness disappeared inside of four hours and patient made an uneventful recovery."

Dr. Pate did not mention having withdrawn any of the mixture at the end of the operation, of having massaged the colon, or of having given postoperative injections of olive oil and water. He did note, however, the naturalness of the sleep, and the numbness or analgesia following a return to consciousness.

ANALGESIA AND ETHER-OIL COLONIC ANESTHESIA.

Drs. Lathrop, Foote, Morton and others have all witnessed and commented on this analgesic state of ether-oil colonic anesthesia. In my own case, before unconsciousness supervened, I distinctly felt a numbness from my waist down, and stated that: "I was ready." The thought at that time was that it was impossible to *hurt* me from the waist down. Dr. Brinckley,[2] states that: "In 2 cases *analgesia* was produced, but *complete anesthesia* was not. One case was a recurrent carcinoma of the face and the other an adenofibroma of the breast. The patients were semi-conscious but felt no pain. In the operaton for carcinoma of the face the Percy cautery was used for one hour and ten minutes. In the breast case the tumor was removed, a frozen section made and examined,— all of which consumed about 35 minutes. The patient would answer any questions asked, but suffered no pain, nor did she remember anything about the operation." It is entirely within the possibilities that a method of *rectal analgesia* may be developed from the perfecting of the technic of ether-oil colonic anesthesia.

PHYSIO-PATHOLOGICAL ASPECTS OF ETHER-OIL COLONIC ANESTHESIA.

In order to induce and conduct an effective administration of ether-oil colonic anesthesia, the anesthetist must have a thorough understanding of the physio-pathological action peculiar to ether dissolved in oil. It is evident from the character of the few adverse criticisms of this method that failures have been due to the fact that certain important physiological factors have received but superficial attention.[3,22]

The course of the circulation of ether in the blood following rectal injection differs markedly from that produced by ether inhalation. A very short time, within 2 to 5 minutes, after the mixture enters the rectum it is heated from room to body temperature; a portion of the ether, at the same time, leaves the oil in the form of gas, which is absorbed by the blood circulating in the small capillaries surrounding the colon. From the colon through the liver, the ether is carried by the greater circulation to the heart, and from the heart it is pumped into the lungs where part is excreted through the air passages and lost, the remainder being immediately reabsorbed and carried on to the brain and the central nervous system. The odor of ether is perceptible in the patient's breath in from 3 to 4 minutes. By the time the anesthetic has reached the lungs it is thoroughly warmed to body temperature.

Effects of Ether Upon the Organism.— There is no irritation to the lungs and mucus and saliva accumulations are usually absent or so small in amount that they are negligible factors in anesthesia. With rectal administration only the ether necessary for narcosis

which is excreted by the lungs goes through the respiratory tract. Therefore, local irritation to the upper air-passages causing a great increase in bronchial secretions which takes place with pulmonary methods is not present in ether-oil anesthesia.

Breathing with this form of anesthesia is perfectly normal. The patient breathes as in natural sleep, so quietly that not even the alae of the nose move, and there is consequently less danger of respiratory arrest than with any inhalation method. Respiratory paralysis, which was promptly relieved, occurred in 2 or 3 experimental cases before the exact dosage had been determined. The reflexes are quite active, especially the lid reflex; at the same time a very great degree of relaxation exists throughout the whole muscular system. The pulse-rate depends upon preliminary medication. When preliminary medication has been given, the pulse is about normal; otherwise, very full and bounding. Usually the face is not flushed, but there is no cyanosis as in inhalation anesthesia. Blood-pressure remains constant.

On account of the large quantity of vapor which is lost by exhalation, the brain is never so deeply narcotized as when the anesthetic is administered by pulmonary methods in which the higher centers of the brain are first affected. In the colonic method the first symptom of anesthesia is sensory paralysis of the extremities and the higher brain centers are the last to be affected, an observation which is verified by the manner in which the patient emerges from anesthesia. Consciousness is regained long before sensations of pain are manifested. This is, no doubt, a strong factor in the wide latitude of safety afforded by this method. With no other anesthetic or method of administration would it be possible to have a patient's respiration cease for 8 minutes and recommence as in one of the cases cited.

AUTOMATIC MAINTENANCE OF ANESTHESIA

When an ether-oil anesthesia is established its depth has been found to be automatically and evenly maintained by four factors acting in harmony: (1), the constant rate of ether evaporation from the oil; (2), the distention of the colon, which permits less ether to be absorbed than when the colon is only partially distended; (3), the cooling of both the mixture and the gut during evaporation, which retards elimination and absorption, and (4), the difference between the ether absorptive power of the colon and the eliminative capacity of the lungs.

In the first place the rate of evaporation of the ether from the oil in accordance with certain inflexible physical laws, conclusively demonstrated experimentally, is always constant in normal individuals. The ether may always be separated from the oil by warming, but unless the temperature of the mixture is suddenly raised to an excessively high point, the ether passes off deliberately. After administering the ether-oil mixture it is impossible at any time to withdraw the oil and leave the ether; or to withdraw the ether and leave the oil. Every molecule of ether is bound to a molecule of oil, and this union is broken only when evaporation occurs. In no other way can their separation be effected. During anesthesia the amount of this vaporization per minute never varies. Therefore it is impossible to have a deep anesthesia at one time and a light anesthesia at another, unless the anesthesia is deepened by rebreathing or lightened by an airway tube.

With regard to the second factor, Sutton found that when the colon was fully distended not so much ether was absorbed as when it was only partially distended. However, the absorbing area of the colon is so much smaller than that of the lungs that a moderate distention of the entire colon is essential to increase its absorbing surface and a sufficient degree of pressure must be employed to obtain this distention. Sutton reports that his attention was first directed to the necessity for the use of a moderate pressure by the repeated observation that reduction of pressure often resulted in deepening narcosis and checking absorption, and that the optimum pressure to be maintained in the colon was determined experimentally to be about 20 millimeters of mercury. That unusual or over-pressure does not occur during ether-oil anesthesia is proved by the degree of distention of the colon and by the absence of distressing after-effects, such as diarrhœa, bloody stools, etc., which attended previous methods of rectal etherization.

In the third place, as the ether leaves the oil in gaseous form, heat is extracted from the surrounding parts and the mixture, as well as the gut, is cooled off in the process. This retards both elimination and absorption and aids in regulating the dose. Pharmacologists, physiologists and surgeons are agreed in stating that etherization produces a general lowering of body-temperature. As loss of heat is a prominent factor in surgical shock, and as surgeons have noted that the ether-oil colon is cold even through a rubber glove, it has been suggested that the possibe temperature loss might prove an element of danger. This frigid condition noted in the colon is the direct result of the evaporation of the ether from the oil. As the ether-oil solution approaches body temperature, ether vapor is given off, which cools the mixture and retards evaporation. This process recurs automatically until all the ether has parted from the oil. In the meantime, the temperature of the patient remains normal, as determined by a thermometer placed in the mouth or axilla. The skin is warm to the touch; the color of the face suggests thorough oxidation. The cold, clammy sweat, sometimes noticed with ether given by other methods, is absent. Furthermore, the question has been raised as to whether this method is not directly opposed to the theory of the administration of warmed anesthetics. Paradoxical as it may seem, the patient under ether-oil colonic anesthesia always inhales a warm, moist vapor. In the course of its circulation from the small blood vessels of the colon through the liver to the heart on its way to the lungs, the ether is moistened and thoroughly warmed to body temperature, a fact which is verified by the absence of lung irritation and bronchial secretions.

The fourth consideration, the difference between the gradual and equal absorption of the ether from the colon and its freedom of excretion from the lungs, obviously acts as a powerful factor in insuring the patient's safety. That these four factors, acting harmoniously, produce as even a plane of anesthesia as can possibly be maintained by any other method is well illustrated by the sphygmographic tracing of a dog under ether-oil anesthesia for one hour during which the pulse and respiratory tracings never varied. This fact was further demonstrated in many hundreds of cases surgically anesthetized by this method in which, without any supplementary anesthetic, the pulse, respiration, reflexes and bood-pressure all remained constant.

THE AMOUNT OF ETHER EMPLOYED.—In the induction of an ether-oil anesthesia the total amount of the anesthetic dose, as estimated by the age, weight and general condition of the patient, must be injected at one time in order to establish the ether tension in the blood essential to surgical narcosis. Objections have been raised to this procedure on the ground that loss of control might ensue. However, it is a fallacy to presume that the total amount immediately is utilized by the patient. If this were so, every ether-oil anesthesia would be accompanied by clinical signs of shock, whereas anesthetization by this method is not only singularly free from such complications, but it is more even in depth than any other form of anesthesia on account of the invariable physiological adaptations which control the evaporation of the ether from the oil. In operations lasting one hour or less, by filling the lower bowel with water and massaging from right to left immediately over the colon, all of the remaining mixture is recovered and the patient regains consciousness in fifteen to thirty minutes. These facts prove beyond all questions that only the amount required to maintain surgical anesthesia is absorbed. Brinkley's contribution as to the amount used is as follows:

"Coburn, in the *Journal A. M. A.*, January 31, 1914, claims: 'The most objectionable feature connected with it is increasing the amount of ether in the circulation; taking the dose for an adult as an example, about 6 ounces of ether plus 2 ounces of olive oil, both by volume, are introduced in the rectum. All of the ether introduced reaches the patient's circulation except that which is subsequently withdrawn, as there is no source of evaporation such as occurs in other methods. It requires only one and one-half ounces of ether in the patient's circulation without rebreathing to induce and maintain an hour's surgical anesthesia. The amount of ether withdrawn in the oil and ether rectal method shows that a much larger amount than this reaches the patient's circulation. Not only does more than 1½ ounces of ether reach the circulation, but there is a decidedly greater tendency toward respiratory paralysis without the corresponding depth of anesthesia that occurs in other methods."

My experience does not bear out Coburn in the foregoing statement. As a matter of fact, we have never failed to get back less than 5½ ounces of an 8-ounce injection, even in cases which were under the anesthetic for an hour and a half. An analysis of the difference between 5½ ounces withdrawn and the 8

ounces introduced amounts to about the same, or less than 1 1-2 ounces per hour, the amount prescribed by Coburn. Of course, a small allowance has to be made for the amount of fluid in the rectum which cannot be withdrawn at the time of administration, but, at the same time, allowance must be made for that amount washed out by the soap-suds solution, so I think they will evenly balance."

Furthermore, most anesthetists and physiologists of today maintain that the *amount of ether utilized by the patient in the maintenance of anesthesia* must always be the same, regardless of the method of introduction. "The ether tension in the arterial blood to the sensorium is the determining factor of anesthetization," (Connell[5]). In order to maintain the same level of anesthesia, this factor must be the same, whether the ether be introduced intravenously, by inhalation, or per rectum.

The amount of the anesthetic employed in this method bears favorable comparison with that employed in all other methods of administering ether. Six ounces of ether with 2 ounces of oil, given to a patient weighing 160 pounds or more, will last nearly 3 hours with even respiration and blood-pressure and constant reflexes. Since the plane of anesthesia is constant, the patient is absorbing about 2 ounces of ether per hour. In two instances in which the operation lasted about three hours, the patient recovered full consciousness, without delirium, within fifteen minutes after being returned to bed, which shows that the 6 ounces of ether was automatically utilized by the patient at the rate of approximately 2 ounces per hour. Only one other form of narcosis requires so small an amount, that is, intravenous anesthesia, which averages 1 1-2 ounces of ether per hour. The drop method is variously reported as requiring 4 to 6 ounces per hour; and the endotracheal, 6 to 8 ounces per hour, that is, more than any other method.

EFFECT OF OLIVE OIL ON THE OPSONIC INDEX.—Olive oil is now used almost exclusively in this method as the cases in which olive oil was used seemed to have less nausea and vomiting than those in which other oils were used. The verification of this statement by other observers would confirm the work of Graham on the restoration of the opsonic index by the absorption of olive oil into the system after the operation.

It is an established fact that ether anesthesia lowers the opsonic index of the blood, that is to say, reduces the power of the patient to resist infection whether of preanesthetic, operative or postoperative origin. Evarts A. Graham[10 11 12] late of Rush Medical College, Chicago, experimenting with fats and other ether-soluble substances in the large intestine of etherized individuals, has shown beyond question that olive oil is capable of restoring to the blood certain properties which are inhibited by the action of the ether, that is, those concerned with phagocytosis. The injection of certain amounts of the oil into the rectum is followed after 3 to 6 hours by a restoration of phagocytic power, although ordinarily depression lasts for several days, while the injection of the same amount of physiological salt solution has no appreciable effect in shortening the period of phagocytic depression. The oil absorbs any ether vapor that may still remain in the intestine and, therefore, not only prevents the protraction of undesirable after-effects but insures speedier restoration of the opsonic index and more satisfactory recovery.

The theoretical objection has been made that the oil might interfere with the anesthetic action of the ether, but I have repeatedly injected olive oil into patients under inhalation anesthesia and can state positively that oil has no effect whatever upon the depth or the course of anesthesia. It certainly does not lessen anesthetic action.

TOXICITY.—Apart from other considerations, the absolutely quiet respiration, the normal pulse rate, the even maintenance of blood-pressure and the presence of good color, all of which are characteristic of an ether-oil anesthesia, would indicate the absence of toxic conditions. Upon withdrawal of the mixture and termination of anesthesia the anesthetic stage merges into one of deep sleep from which the patient awakens gradually and as easily as from natural slumber. The absence of nausea and vomiting in the majority of cases with no change in the urine, the blood, or the mucous membrane, as determined by the proctoscope, the fact that ether vapor colonic anesthesia was used by Sutton and Brewer for patients with impaired organs, as well as the fact that ether-oil anesthesia is now being successfully used in one hospital *only* in desperate cases in which inhalation anesthesia

might prove dangerous, are further indications that there is less toxicity during ether-oil anesthesia than with the usual inhalation methods.

DEATH.—Theoretically, fatality is less likely to result from this method, since the lungs are free to eliminate ether as fast as it is absorbed from the rectum, but undoubtedly, deaths will occur with ether-oil, as with other anesthetics, if administered when contraindicated or with faulty technic. Certainly it should never be administered in borderline cases unless the physiology is thoroughly understood. However, no deaths can properly be accredited to this method, although one patient among the early cases did succumb within twenty-four hours after the administration of the anesthetic. This patient had regained consciousness and had fully recovered from narcosis. The coroner's inquest revealed the fact that every organ in the body was diseased, and that a vegetating growth completely obstructed one of the coronary arteries. In the opinion of the surgeon and the coroner, these conditions fully accounted for death. No other fatalities have resulted, except one death reported through the courtesy of Dr. H. Clifton Luke, of St. Luke's Hospital, New York City, which, in his opinion, was attributable in a measure to the anesthetic.

CASE OF DR. H. C. LUKE.—Operation, jaw resection. "A fairly vigorous man of about fifty years; really never recovered from the anesthetic, and was in a most profound state of narcosis for nearly six hours. Six ounces of ether and two ounces of olive oil were administered in the usual manner, and both before and after the operation was completed, the colon was repeatedly irrigated without apparent benefit. Patient died with an aspiration type of pneumonia 22 hours after operation."

That Dr. Luke employed an imperfect technic in this case is obvious from his patient's tardy recovery from the anesthetic. No mention is made in his report either of the use of chloretone or any other hypnotic, or even of the hypodermic of morphin, which I have always prescribed in every article I have presented on the subject. The fact that "the colon was repeatedly irrigated without apparent benefit" indicates that too much of the solution was injected in the first place, and that irrigation should have commenced even before the operation. As a last resort, an intravenous saline injection of about 1,000 to 2,000 c c., should have been administered. A "most profound state of narcosis for nearly six hours" means an overdose, an imperfect airway, or both; for it has been repeatedly demonstrated that 8 ounces of a 75 per cent. ether-oil mixture will keep a patient of 160 pounds or over in surgical anesthesia for three hours, and no longer, provided a clear airway is maintained. The occurrence of "an aspiration type of pneumonia" is partly due to the anesthetist's failure to keep a clear airway by sponging or by using a suction apparatus.

The theoretical objections to ether-oil based upon such a faulty technic may prove misleading, but they really bear little weight in comparison with the clinical results in many hundreds of successfully conducted ether-oil anesthesias. With improvement in technic, however, no untoward results have been recorded.

AFTER-EFFECTS.—In ether-oil colonic anesthesia undesirable after-effects are reduced to a minimum and compare most favorably with the postanesthetic sequelae of routine methods of ether and chloroform administration. In fact, it has been demonstrated, in over 1,000 cases, that the dangers and discomforts which usually attend inhalation anesthesia, including nausea, postether pneumonia and renal injuries, are practically absent.

Brinckley[2a] writes as follows about one of his patients:

"This patient was a very intelligent woman. She had taken ether by inhalation 4 times previously and said she would suffer a great deal with nausea and vomiting at the beginning of every anesthetic and this would persist for from 2 to 3 days afterwards. With ether and oil rectal anesthesia she suffered with neither at administration, nor other discomfort. She had no nausea whatever after the first 6 hours. She said she would never care to take an anesthetic any other way."

The complictions incident to intravenous anesthesia, thrombosis, embolus and infection, are also eliminated by this method of induction, and the difficulties encountered in other methods of rectal etherization, such as diarrhœa, bloody stools or blood-streaked returns, do not follow ether-oil colonic anesthesia. This procedure has been used in anesthetizing consumptives, asthmatics and patients with bronchitis and in no instance has the condition of the patient been aggravated.

THE TECHNIC OF ETHER-OIL ANESTHESIA.

APPARATUS.—The simplicity of the equipment required for this method is a decided

point in its favor. The only apparatus used is a special rectal tube or catheter one-quarter of an inch in diameter and about 28 inches in length; a clamp for this tube; a 3-inch glass funnel with which to introduce the ether-oil solution; a Gwathmey tube about 30 inches long and three-eighths of an inch in diameter with which to flush or remove fluid from the rectum; and a towel which is placed over the face of the patient from time to time to prevent dilution of the anesthetic in the air-passages until narcosis is complete. A pharyngeal air-way tube should be convenient, to lengthen the anesthesia if necessary. Of course, the tubes should be sterilized before use.

DOSAGE.—In using the ether-oil method, the anesthetist must bear in mind the peculiar physiological effects of the ether-oil mixture in order to avoid errors in administration. From a large number of cases we have now deduced the rule of one ounce of a 65 per cent. solution of ether in oil for every 20 pounds of body weight in the normal adult and *this amount and this percentage should never be exceeded.* This amount compares favorably with that employed in all other methods of administering ether. Age, weight, fever, anemia and general weakness modify the dosage as in other methods of general anesthesia, and, by diminishing the amount of the mixture administered in accordance with these factors, overdosage may be readily controlled. A 50 to 65 per cent. solution is sufficient for children and weak, anemic patients.

For Patients Under Six Years.—A 50 per cent. solution should be employed. This mixture is non-irritating, is easily retained without preliminary medication, and is followed by satisfactory anesthesia in 10 to 20 minutes. A child 4 to 6 years of age would probably require just a little more than one ounce for every 20 pounds of body weight. No risk should be incurred with children because the rate of evaporation is much more rapid than in the case of adults. The mixture may be administered very slowly and from one-half to one ounce may be added later, if necessary.

For Patients From Six to Twelve Years.—A 55 to 65 per cent. solution is used without preliminary medication. One ounce is administered for everey 20 pounds of body weight, and 20 to 30 minutes should be allowed for the anesthetic to have full effect.

For Patients From Twelve to Fifteen Years.—One ounce of 55 to 65 per cent. solution to every 20 pounds of body weight should be administered, with the possible addition of 1-12 grain of morphin and 1-200 grain of atropin given hypodermatically as a preliminary.

For Patients of Fifteen and Upwards.—A 65 per cent. mixture is injected, the amount and preliminary medication varying with the size and genereal condition of the patient and the same rule being followed as to quantity, that is, one ounce for every 20 pounds of body weight, except for the obese patient. Six ounces of a 65 per cent. solution, that is, the usual dosage for the average case, will maintain anesthesia from 2 1-2 to 3 hours, provided a clear airway is maintained. *No more than 8 ounces should ever be given.*

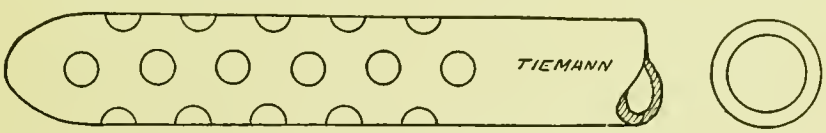


FIG. 180.—GWATHMEY RECTAL IRRIGATION TUBE.

For Weak, Anemic Patients.—The mixture should consist of olive oil, 35 to 45 per cent., and ether, 55 to 65 per cent.

Preliminary Treatment.—A cathartic of castor oil should be given, preferably the night preceding the operation, and repeated the following night, and purging should be avoided. This should be followed the morning of the operation by warm water enemas, one hour apart, until the return is clear, when the patient should be permitted to rest for 2 or 3 hours.

The quantity of preliminary medication depends largely upon the opinion of the surgeon or anesthetist, and will vary with this method as with other methods of administration. No preliminary medication is required for children under 9 years of age, but, in order to

obtain the most satisfactory results with adults, preliminary medication is essential, with a rest in bed of 2 or more hours before injection. As the preliminary, either chloretone or paraldehyd may be used, since both have been found to diminish the amount of the anesthetic required and to assist materially in guaging the susceptibility of the patient to this form of anesthesia. Other hypnotics of equal value may be substituted for them if preferred. Isopral, also, has a slight local analgesic, as well as a general hypnotic effect, and may prove satisfactory.

Technic With Chloretone.—One hour before operation visitors should be excluded, the room darkened, and quiet maintained. With the patient in the Sims position, give per rectum 5 to 10 grains of chloretone in a suppository, or dissolved in 2 to 4 drachms of ether mixed with an equal amount of olive oil. Fifteen minutes after the chloretone inject hypodermatically 1-8 to 1-4 grain of morphin, with 1-200 to 1-100 of a grain of atropin, the larger doses are given only to athletes and alcoholics, for whom the method of medication differs as follows: Two hours before operation give 1-100 grain of hyoscin hydrobromid hypodermatically, and one hour before operation repeat the hyocsin with 1-4 grain of morphin, omitting the rectal preliminary.

Technic With Paraldehyd.—When paraldehyd is used in connection with ether it intensifies the action of the drug and insures more complete relaxation without in any way affecting the pulse or respiration, and by employing it as a preliminary with this method the usual amount of ether-oil solution may be reduced one-third to one-half. One drachm of paraldehyd used in this way seems to be equivalent in anesthetic value to 2 ounces of a 75 per cent. ether-oil mixture, which was the solution formerly used.

One hour before operation administer a solution of 1-8 grain of morphin, 1 to 2 drachms of paraldehyd, and 3 1-2 drachms of ether and olive oil in equal parts. This one-ounce solution takes the place of the chloretone only, in the technic previously described. In other respects that technic should be followed except in the case of athletes, alcoholics and patients weighing over 160 pounds. For these patients, instead of the morphin and atropin hypodermic, the paraldehyd solution should be repeated. For the average patient do not repeat the dose. This procedure has proved so satisfactory that now no more than 2 drachms of paraldehyd are ever used for any patient.

This paraldehyd mixture, when used as a preliminary to nitrous oxid and oxygen, renders any further addition of ether by inhalation unnecessary, gives a greater relaxation, and the ether and paraldehyd are not noticeable to the patient.

The Use of Local Anesthetics.—The question of whether or not a local anesthetic should be used at the site of the operation is a matter for the surgeon himself to determine. Where my opinion is asked, I advise its use unless it is contraindicated by special conditions.

Administration.—The Patient.—The administration of ether-oil colonic anesthesia is best accomplished with the patient in his own bed, lying on the left side, in the Sims position. A convenient lifter should be placed under him before beginning the injection. If the bed is in a ward, it should be screened and exposure of the patient avoided by introducing the rectal catheteer between two suitably adjusted sheets. A pillow under the hips is sometimes helpful. It is not always necessary that he should even know that an anesthetic is being administered but, in any event, he should be kept perfectly quiet and should never be left alone at any time after having received the injection.

Induction.—20 to 30 minutes before operation the ether-oil mixture is poured very slowly, allowing about one minute for the introduction of each ounce, through the funnel attached to the rectal tube which has been well lubricated, and filled partly with oil, inserted 4 inches within the rectum and clamped. At the very least 5 minutes should be consumed in administering 6 ounces, which is the usual amount required. Unconsciousness generally follows in from 5 to 10 minutes after the completion of the injection and, except in rare cases, full surgical narcosis is reached in from 10 to 30 minutes.

If the patient goes to sleep before the required amount has been given, STOP ! If narcosis is delayed a few whiffs of ether or chloroform may be used.

It is advisable not to withdraw the catheter

until the patient is partly unconscious and the muscles are relaxed. From 5 to 20 minutes, in accordance with the percentage used, should be allowed for the anesthetic to take effect before the patient is moved to the operating-room.

Maintaining Anesthesia.—After the patient has received the mixture a clear airway must be constantly maintained by placing a finger beneath the symphysis of the lower jaw. Care must be exercised to prevent the air-supply from being cut off, either by the head falling forward or sidewise, or by the tongue falling backward. If the breathing is easy and regular, with the reflexes active, the patient will be found to be completely relaxed and in surgical narcosis as long as the operation lasts. Six ounces of the 65 per cent. mixture will last from 2 1-2 to 3 hours. If the operation is completed before this time, the Gwathmey tube should be inserted in the rectum beside the catheter and as much of the mixture drawn off as possible.

The physiological changes incident to this method will be found to result in the automatic maintenance of surgical narcosis. The anesthetist has complete control of the anesthesia at all times, and any error in judgment as to the proper amount of the solution in the first place may be quickly rectified by either the addition or withdrawal of the mixture. If the patient shows undue susceptibility to the ether, part or all of the mixture may be withdrawn immediately, if necessary. On the other hand, if the patient seems too lightly narcotized with the regulation dose, anesthesia may be deepened by a few drops of ether or chloroform on the towel, which is preferable to increasing the amount of the solution; or it may prove sufficient to prevent the dilution of the anesthetic with the outside air by placing over the face a towel slightly puckered just above the nose and mouth, but held securely to the face around the edges, so as to inhibit the escape of the ether vapor and induce a certain amount of rebreathing. Anesthesia may be concluded at any time by placing a Gwathmey tube in position and massaging over the colon from right to left to expel the remaining mixture. When anesthesia is so terminated, the anesthetic stage merges into one of deep sleep.

Fig. 181a.—Showing Patient in Position for Oil-ether Administration.

Danger Signs.—If a mistake in judgment as to the amount is made, it is manifested in about 15 minutes. Slight cyanosis, a diminution in the activity of the reflexes, or the occurrence of stertor or embarrassed respiration of any kind, except in very stout persons in whom a slight stertor or even a puffing of the lips is not necessarily a danger signal, is an indication that the narcosis is becoming too profound. If any of these symptoms evince

themselves, 2 or 3 ounces of the mixture remaining in the colon should be withdrawn immediately through the Gwathmey tube placed 4 to 6 inches up the rectum beside the catheter, and if the symptoms persist, the rectum should be irrigated with cold water and the sphincter stretched. If this does not remedy the trouble immediately, introduce a Connell breathing tube and transfuse 1,000 to 2,000 c.c. of normal saline intravenously.

If respiratory arrest occurrs a bag filled one-third full of carbon-dioxid gas is placed over the face, and the condition remedied with artificial respiration. With this method, as well as all other methods of administration, the chief danger lies in respiratory arrest as shown in representative cases cited. No other cases have occurred in my own practice or been reported by others.

However, even though conditions seem ideal under ether-oil colonic anesthesia—that is, the color of the patient is good, the skin is warm to the touch, the reflexes active and the pulse normal, with complete absence of stertor and even of the puffing so frequently observed under inhalation anesthesia—watchfulness must be exercised at all times. The very simplicity of the method may lead the inexperienced to attempt its use without adopting the precautions which must be observed in order to make this or any other method of general anesthesia a safe one. Such explicit directions may seem superfluous, but in view of the deplorable lack of knowledge of anesthetic administration among the internes in our hospitals at the present time, the author considers them essential.

When the ether-oil solution is injected in accordance with the fixed rules outlined herein, it is physically impossible to shock the patient either at the time of introduction of the anesthetic or during anesthesia.

Postoperative Treatment. — Immediately upon conclusion of the operation the clamp on the catheter is released, and the end lowered so that the residual mixture is syphoned off. The Gwathmey tube is inserted into the rectum to a depth of about 6 inches, or as high up the colon as is convenient without traumatism, alongside the catheter. About one gallon of cold soapy water is now poured through the funnel attached to the catheter, and is syphoned off by the Gwathmey tube. At the same time, in order to expel any liquid that may remain, the colon is massaged gently from right to left. The Gwathmey or large rectal tube should now be withdrawn. Two to four ounces of olive oil should then be introduced into the rectum followed by one pint to one quart of water, and the catheter now withdrawn.

Brinkley's technic for emptying the lower bowel is probably the best:

> "About 5 minutes before the end of the operation a large rectal tube is introduced and all the mixture is siphoned off; then a Y-shaped tube is connected with the rectal tube at the stem of the Y, with the irrigating can in which the soap-suds solution is contained connected by one arm, and a rubber tube for siphonage with the other. The siphonage tube is clamped and the bowel distended with about one pint of the soap-suds solution. Then the tube is unclamped and the solution siphoned off. This is repeated until the solution returns with no signs of the mixture in it, abdominal massage being performed over the colon to help empty the bowel. Then, from 2 to 4 ounces of olive oil is introduced and the tube withdrawn. The patient is carefully returned to bed. The room is darkened and well ventilated. Cold Saline enemas, 12 ounces every 4 hours, are ordered. With the foregoing technic we have had not a single case of proctitis nor has there been any complaint of rectal discomfort following the anesthetic."

The reflexes should then be quite active and the patient breathing quietly. Further after treatment is the same as in other forms of anesthesia. The patient should be returned to bed with as little jolting or handling as possible, the room should be darkened, and free ventilation established. The patient usually recovers consciousness in from 30 to 50 minutes after this procedure, quietly, without nausea, vomiting or pain, and analgesia continues for some time after consciousness is restored.

Technic For General Practitioners.—It would be safer for a practitioner, who must work unassisted, to use a 55 to a 65 per cent. solution of ether and oil, to allow 15 to 30 minutes for the mixture to have its full physiological effect, and then to supplement this dosage, *if necessary*, with a few drops of ether on a mask. This procedure would be better than inducing profound anesthesia with a 75 per cent. solution, with the possibility of having to withdraw some of the mixture if the patient was too deeply narcotized. This combined method would also be a safer one for use by hospital internes and others who have

not had extensive experience in the administration of anesthetics.

LUMBARD'S TECHNIC.

Dr. Joseph E. Lumbard, Instructor in Anesthesia, University and Bellevue Hospital Medical College, and Anesthetist to the Harlem, Knickerbocker and Lying-in Hospitals, New York City, earnestly commends this method, especially in surgery of the head and neck. In 36 head and neck operations, including 10 thyroidectomies, cleft palate, cancer of the tongue and neck, Jacksonian epilepsy, tuberculous glands of the neck, radical mastoiditis, tumor of the brain, fractured skull, goitre and carcinoma of the pharynx, Lumbard used ether-oil colonic anesthesia with marked success. The average pulse rate in the 36 cases, was 87 per minute; the average respiration, 21 1-2. The length of the operations varied from half an hour to two hours. The quantity of the mixture employed, 25 per cent. olive oil and 75 per cent. ether, was from 180 to 230 cubic centimeters. There was no disturbance of pulse or respiration. The time of recovery after operation varied from one-quarter of an hour to three hours. There was no nausea or vomiting in 28 cases, that is, in 80 per cent. The patients in two instances had been previously anesthetized by the usual inhalation methods and both were emphatic in their preference for the rectal method.

"To anesthetize an aggravated case of exophthalmic goiter without the patient's knowledge, to maintain surgical anesthesia with a normal pulse and respiration, and to keep the upper air-passages free from mucous secretions is one of the most difficult tasks confronting the anesthetist. This can be done with ether-oil anesthesia. Having had 90 cases (with 18 different surgeons) I feel justified in recommending the extended use of this method in head and neck operations. Have never known of any rectal irritation following it."

In a report on these cases in *Surgery, Gynecology and Obstetrics*, Lumbard outlined his administrative technic and its variations from that of the author, in brief, as follows:

Preparation of the Patient.—Keep the patient in bed in a quiet darkened room until the anesthetic has been administered and he is ready for the operating room. A few hours before operation clear the bowel moderately with a compound of licorice powder. Two hours before operation irrigate the bowel with plain water until the return is clear. Introduce a large rectal tube, have the patient assume the squatting position, and with slight massage of the abdomen insure the complete emptiness of the lower bowel. One-half hour before administration give a hypodermic of morphin and atropin. Thirty minutes after the hypodermic place the patient on the left side with the knees well drawn up. About three inches into the rectum, introduce a small, well-oiled, soft rubber catheter, with a funnel attached.

Induction.—Use three parts of ether and one part of olive oil, by measure. *It is very important to mix the solution thoroughly by shaking it in a bottle for one minute.* Introduce the mixture very slowly, one fluid ounce to every 20 pounds of body weight, having the nurse pinch the catheter so that the injection takes about five minutes. During the injection it is not necessary to introduce the catheter more than three inches or to hold the funnel more than one foot above the level of the rectum. Slowly withdraw the catheter and prevent expulsion of the anesthetic by constant pressure over the anus with a hard-rolled bandage. This is a technical detail of importance. Ether will be detected on the patient's breath in from 3 to 5 minutes followed by surgical anesthesia in from 5 to 20 minutes. Remove pressure over the rectum and carry patient on a stretcher to the operating room.

Maintaining Anesthesia. — Should anesthesia be delayed over fifteen minutes place a wet towel over the face and, if necessary, give a few whiffs of nitrous oxid or ether by the closed method. In case of overdosage empty the rectum immediately by means of a large rectal tube having perforations at the sides and one at the end. Incline the operating-table with the head up while massaging the abdomen and establishing a free airway with a Lumbard controller of the tongue and palate. Should respiration cease, use artificial respiration and forced breathing of equal parts of carbon dioxid and oxygen.

Postoperative Treatment.—Empty the rectum during the last part of the operation. On

the patient's return to bed, irrigate the bowel with tepid water until the return shows none of the mixture and introduce 3 ounces of olive oil to be retained.

Points of Difference From the Author's Technic.—This technic differs from the author's in four respects. The oil is not used for a cathartic before administration, no preliminary bowel medication is employed, the ether and oil are mixed in a bottle by shaking rather than in a graduate, and a plain water instead of a soapsuds enema is used.

Advantages.—The advantages of the method, which Dr. Lumbard states briefly as follows, are practically a confirmation of many of those claimed for the method of the author: In head and neck operations hemorrhage is less and the anesthetist is out of the way; the possibility of anesthetization without the patient's knowledge, which is of great advantage in operations for exophthalmic goiter and in operations on the nervous and the insane; the elimination of dread; the absence of excessive mucous secretions, which is a great factor in bronchoscopy; the fact that pulse and respiration are more normal than with any other method of general anesthesia; the elimination of the inhaler; the simplicity of the apparatus; the reduction of nausea and vomiting; and the absence of postanesthetic excitement.

LATHROP'S TECHNIC.

One of the most enthusiastic adherents of this method, Dr. Walter Lathrop, of the State Hospital, Hazleton, Pennsylvania, in a paper on "Rectal Anesthesia in Thyroidectomy," read before the Pennsylvania State Society, September 22nd, 1915, reported having used ether-oil colonic anesthesia in 155 cases, between June, 1914, and September, 1915.

In the goiter cases, as well as in other operations conducted under ether-oil colonic anesthesia, Dr. Lathrop reports an even plane of anesthesia, with complete relaxation and little or no change in blood-pressure. Pulse and respiration as a rule remained near normal, or did not vary much from their condition when the operation was commenced. If rapid, as in hyperthyroidism, they remained rapid but, owing to the absence of fear with this method, did not grow more so. The eye reflex was seldom lost.

Postoperative effects were much better than with inhalation anesthesia. Vomiting was present in less than 12 per cent. of the cases. There was only one case of looseness of the bowels in over 150 administrations, and only one case in which any of the mixture had to be withdrawn. Patients regained consciousness rapidly after flushing of the colon, were usually comfortable aside from the unavoidable throat irritation following goiter surgery, and could retain medication or nourishment. In abdominal operations there was usually freedom from pain for some time after the patients were returned to bed, although consciousness had been fairly well regained.

Dr. Lathrop commends the method especially for goiter cases, for neurotics, for patients with asthma, for hernia operations, *"on patients such as we see in the coal regions, who suffer with miners' asthma,"* for fat patients with short, thick necks and narrowed air-passages, and for all operations on the head and neck; but he especially emphasizes its usefulness in thyroidectomy, where the absence of the ether cone gives freedom of movement to the surgeon, and when the patient may be anesthetized with little conception of what is taking place.

"How helpful this is anyone who has seen many cases of high-strung, nervous, apprehensive hyperthyroid cases, or those who have not yet reached the toxic stage, but are near enough to be exceedingly nervous or depressed, can fully appreciate."—LATHROP.

Technic.—The technic employed by Dr. Lathrop is a distinct advance, inasmuch as he never uses over 6 ounces of a 65 per cent. solution.

Preparation of Patient.—The night preceding operation a laxative is administered, usually calomel or phenolphthalin, followed in the morning by enemas, usually two, an hour apart, using plain, warm water, or a weak suds solution.

Apparatus.—A special rectal tube is used one-quarter of an inch in diameter, with an eye on the side and a small funnel into which to pour the mixture. During anesthesia the rectal tube is left in the bowel and clamped.

Preliminary Medication.—Morphia, 1-4

grain, and paraldehyd, one or two fluid drachms; ether and olive oil of each 4 fluid drachms, are given 40 minutes before the operation, followed in 20 minutes by the ether-oil mixture. Morphia is never given hypodermatically.

For Children: No preliminary treatment aside from the laxative and enema, is prescribed for children under 10 to 12 years.

For Alcoholics.—Rectal preliminary is omitted. Two hours before operation 1-100 grain of hyoscin is given hypodermatically. One hour before operation this is repeated with the addition of 1-4 grain of morphin, after which the ether-oil solution is introduced.

For Hyperthyroid Cases.—A small injection consisting of 4 ounces of plain water is given every second day for a week preceding operation with instructions to the patient to retain it for its tonic effect. Brinckley's technic in exopthalmic goiter cases varies slightly from Lathrop's: "In exopthalmic goiter cases a small soapsuds enema *with a few drops of ether* is given every morning for 3 or 4 mornings before the operation, explaining that this is part of the treatment and that you want them to retain the enema for a short while. *The few drops of ether are added in order to accustom these patients to a slight odor of it.*"

Administration.—"It is important that the use of the ether-oil mixture be in the hands of one who can begin its administration, and have it under his or her care in all cases, and not delegated to a different doctor, or nurse, each time it is used."—LATHROP.

The mixture is usually given with the patient in the Sims position on the table, for the patient is drowsy and does not realize what is taking place, "but some women will require the entire anesthetic procedure in bed before removal to the operating-room."

The dosage for nearly all adult cases is ether, 3 ounces by measure, and olive oil, 2 full ounces. This is less than was formerly used, but, by giving 1 drachm or 2 of ether by inhalation in case the patient is not quite asleep, the resulting anesthesia proves perfectly satisfactory. For children the anesthetic solution consists of equal parts of oil and ether.

Maintaining Anesthesia.—"Should narcosis be slow, or the patient restless, as will occur now and then, a few whiffs of ether will quickly produce sleep, usually one or two drachms is ample." A piece of gauze is kept over the nose and mouth.

Postoperative Treatment.—While the sutures are being introduced, the rectum is thoroughly irrigated with tap water or soapsuds, and any mixture that may remain is expelled by gently massaging the colon from right to left. Four ounces of olive oil and one pint of water are then introduced and allowed to remain. The patient usually sleeps quietly for from 2 to 3 hours but can easily be aroused and is seldom troubled by vomiting.

Recently, in a personal communication, Dr. Lathrop announced that his ether-oil administrations in neck and abdominal operations now number 200; that in the case of an asthmatic patient with double inguinal hernia, in which the hernia was enormous and had been out for 2 years, the use of ether-oil was followed by excellent anesthesia. In cases of dilatation and curettment, followed by laparotomy with absolute perfection of anesthesia, he notes especially that the rectal tube was not removed. It was simply supported to prevent its slipping out, and its position did not inconvenience the surgeon in any way.

INDICATIONS.

It has now been demonstrated conclusively that the lives of certain types of patients are better safeguarded by the employment of ether-oil colonic anesthesia than by any other method. For certain subjects and operations it has proved to be the least hazardous and the best method from every point of view. It is especially indicated in the very obese, regardless of the nature of the operation, both on account of the difficulties encountered with inhalation methods in individuals having narrowed air passages, and on account of the affinity of fats for oil. For the obese any inhalation method is fraught with risk; spinal and local anesthesia are difficult; intravenous anesthesia is less objectionable but is also attended with difficulty in this type of patient. With ether-oil administration, however, these patients enter surgical narcosis easily and awaken as from natural sleep. In every instance of this kind the nausea is negligible.

For neurotics, the insane, and those in whom the physic element predominates, this method is also especially adapted.

It has been found ideal where the element of fear is as potent a factor as it is in goiter cases, especially in hyperthyroidism, and in all operations upon the respiratory tract, head, neck and chest, where the presence of an ether cone is a hindrance to the surgeon as well as a source of possible infection. It is the best of all methods in the surgery of the upper air-passages and in cases where the patients are already suffering from respiratory embarrassment. In such cases the anesthetist is free to assist the surgeon by using a suction apparatus for blood, without at the same time lightening narcosis by withdrawing the ether vapor, as would occur in all inhalation anesthesias, except endotracheal anesthesia, a method which, in the writer's opinion, should never be resorted to unless positive pressure in the lungs is essential.

It is especially indicated in esophagoscopy, as demonstrated in the experience of Dr. Hubert Arrowsmith, of Brooklyn, and in suspension laryngoscopy, bronchoscopy and gastroscopy, where the absence of excessive mucous secretions in the air-passages is a valuable factor. In these cases the patient is further safeguarded by having a clear passage for the exit of ether vapor. This airway lightens the anesthesia very little and the introduction of the instrument prevents the possibility of its growing too profound. Furthermore, with this method, the patient does not *crawl* as the instrument is introduced, nor is the focus liable to disarrangement at any time.

It has also been demonstrated in practice that the method may be used, with perfect results and no inconvenience to the surgeon, in many abdominal operations, including hernial reductions and laparotomies.

Since ether proves less irritating when given in this way, it may be administered with confidence to those patients who have suffered nausea and vomiting from previous inhalation etherization.

Its field of usefulness is further extended by its value in cases where absorption must be minimized on account of lung, heart or kidney lesions. It may be given without deleterious effects to patients suffering from tuberculosis, pulmonary abscess, pneumonia, empyema and mediastinal abscesses.

CONTRAINDICATIONS.

Ether-oil colonic anesthesia should never be employed in diseased conditions of the intesetines. Pathological conditions of the lower bowel, such as colitis, hemorrhoids, ulcer and fistula in ano, are positive contraindications to the method, and it is important to ascertain this point. The introduction of the ether-oil solution is aggravating to intestinal lesions, especially in cases where the intestinal walls have been weakened by disease, and there is a possibiity of resulting perforation of the gut. Even where no lesion is known to be present, if there is considerable rectal pain upon introduction of the solution, rectal anesthesia should be discontinued. Furthermore, whenever ether is contraindicated, ether- oil is also contraindicated, except in bronchitis, asthma, and similar conditions which have been noted heretofore. If, however, the patient has suffered nausea and vomiting during a previous ether narcosis, ether-oil anesthesia may be conducted with confidence.

Finally, owing to the necessity for preliminary preparation of the colon, this method is contraindicated, as a rule, in emergency cases.

ADVANTAGES.

From an extended personal experience, as well as that of a large number of surgeons and anesthetists, and from a critical review of all the available data on ether-oil colonic anesthesia, I feel sure that the following advantages may be justly attributed to the method.

Safety.—(1) In ether-oil colonic anesthesia the limits of safety are wider than with any other known method, as evinced in the difference between the dosage required for surgical narcosis and that which precipitates toxemia. The fact that it requires from 10 to 20 minutes for the anesthesia to fully assert itself would also indicate that an equal time would be given, if any undesirable symptoms should present themselves, and that is exactly what occurs. This is well illustrated in the case in which a near-fatality resulted. The

patient received 4 times the required preliminary medication and two-thirds more of the mixture than is necessary, with a resulting respiratory arrest of 8 minutes. Upon instituting the usual restorative measure, she made an uneventful recovery. (2) The safety of this method is further assured by the fact that the lungs are free to eliminate ether as fast as it is absorbed from the rectum and that, owing to the large quantity of vapor which is lost by exhalation, the brain is never deeply narcotized. (3) When the technic outlined by the author is adhered to, both preanesthetic and surgical shock, so far as the anesthetic is concerned, are almost impossible. (4) Postoperatively, the ether-oil solution acts as a prophylactic against colon baccillus infection. (5) In head and neck surgery, the operative field is free from contamination by the anesthetist. (6) While the total amount of the mixture is in the body, the patient is as safe from an overdose as if it were in a container outside the body. (7) No deaths may be directly attributed to this method.

Comfort.—(1) With the ether-oil method patients are anesthetized in bed with little or no conception on their part of what is taking place. The administration is conducted without the slightest exposure of the patient. (2) The patient lies on the left side in perfect comfort, in marked contrast to the disagreeable supine position required for anesthesia by inhalation. (3) The apprehension of impending danger usually caused by placing a mask over the face is avoided and the patient enters surgical narcosis easily and rapidly with no sense of suffocation. (4) In operations where the element of fear is a dominant factor, in the presence of insanity or of nervous tension, the pre-operative control of mental distress and excitement by this method has proved invaluable. (5) The comfort of the patient is further enhanced by the fact that he awakes in an analgesic state and postoperative pain is eliminated.

Control.—Owing to certain physiological factors which have been defined, narcosis is automatically maintained at a more even plane than is possible with any inhalation anesthetic, unless administered by a skilled anesthetist using a perfected apparatus. The anesthetist always has complete control of the anesthesia. Any error in judgment may be quickly rectified by the addition or withdrawal of the mixture, or anesthesia may be terminated at any time by withdrawal of the mixture.

Efficiency.—(1) This method insures prevention of shock. (2) Narcosis is smooth and of uniform depth. (3) Pulse and respiration remain near normal, without mucous râles. (4) There is little or no change in blood-pressure. (5) The reflexes are not disturbed. (6) A more complete relaxation of the general muscular system is secured than with any other known method. (7) The stage of excitement characteristic of inhalation anesthesia is eliminated. (8) The patient always inhales a warm, moist vapor, and the direct irritation of a concentrated vapor is overcome. (9) Loss of heat is minimized during operation because of the diminished sweating and ether refrigeration with this method. (10) In over 95 per cent. of cases there is no eructation of gas during or after anesthesia. (11) Hypersecretion of mucous and saliva is absent, for the ether-oil is less irritating to the colonic mucous membrane than ether vapor is to that of the respiratory tract. (12) The absence of the ether cone in surgery of the head and neck not only lessens the technical difficulties of the operation by giving continuous access to the field of operation, but also considerably lessens the duration of the operation. (13) There is also less hemorrhage in head operations. (14) The patient's stomach, lungs and kidneys are spared. (15) As a partial analgesic, ether-oil injection is the best preparation for local analgesia. (16) Furthermore, this method not only does away with many of the dangers of inhalation anesthetics, but avoids thrombus, embolus and infection, the chief dangers of intravenous anesthesia.

Simplicity.—(1) The apparatus required is inexpensive and the simplicity of the technic enables the anesthetist to devote his entire time to the patient. (2) It is the safest and simplest method for use by the practitioner who must work alone, for inexperienced hospital internese or in the hands of the layman compelled by circumstances to administer anesthesia.

After-Effects.—(1) With normal patients such complications as colitis, bloody stools, or

blood-streaked returns do not occur. (2) There are no toxemic complications. Blood and urine analyses, as well as clinical symptoms, fail to reveal any toxicity due to this method. (3) The distressing after-effects of inhalation ether anesthesia are absent. This is especially true of vomiting. (4) Postoperative nausea as well as gas pains are reduced to a negligible quantity, and there is no postoperative pneumonia.

These conclusions have been based upon the actual demonstration of the advantages claimed for the method in over 1000 *cases, in patients of all ages, under the care of various surgeons, who are enthusiastic in expressing their unqualified approval of ether-oil colonic anesthesia.*

Freudenthal's Report.—Dr. Wolff Freudenthtal, laryngologist, New York City, says in part in *Archiv für Laryngologie und Rhinologie*:

"Every laryngologist has experienced the difficulties of operating under general anesthesia with repeated interruptions due to the ineffectiveness of the anesthetic, and everyone knows how unpleasant are the after-effects, even in minor operations, not to mention the increased danger of infection from the anesthetist himself . . I have tried nearly all methods in the last few years, Kuhn's peroral intubation, Meltzer's intratracheal insufflation, the administration of ether through a catheter in the pharynx or nose, and intratracheal insufflation with the Charles Elsberg apparatus, which has rendered extraordinary service in my clinic . . . But, in spite of all the advantages of the latter method, the fact that it has certain faults must not be lost sight of . It was, therefore, with pleasure that we welcomed an entirely new method, and immediately experimented with it in our clinic ."

Dr. Freudenthal saw ether-oil anesthesia in use for the first time in the clinic of Dr. Hubert Arrowsmith, of Brooklyn, and from his own experience in a number of cases, as well as his observations in the office of Dr. Arrowsmith, he reports the following results with ether-oil as an anesthetic: Rapidity and ease of induction; the reflexes, especially the lid reflexes, always present; no nausea or distress; absolutely quiet sleep; no suffering from shock; and no postoperative disturbances. In two cases in which there was restlessness due to insufficient preparation, anesthesia was supplemented with chloroform and proceeded successfully. In operations on children the results were disappointing, but he attributes this to limited experience rather than to any fault in the method, and further states that, in spite of the fact that there were occasionally slight difficulties to be overcome, "*at all times the new method excelled the inhalation method.*"

Case I.—Child; age, 9 years. Inferior tracheotomy for removal of a foreign body from a bronchial tube. Operation by Dr. Arrowsmith. Pneumonia had already set in. It took one and a half hours to locate the trouble without the child's regaining consciousness. No attention was paid to the anesthetic after it had begun to take effect. Repeated cyanosis resulting from the interference with respiration was relieved by removing the bronchoscope and insufflating oxygen.

Case II.—A strong young man. Operation for nasopharyngeal fibroma by Dr. Arrowsmith. Anesthesia proceeded smoothly.

Case III.—Girl; age, 20 years. Operation for cleft palate by Dr. Arrowsmith. Barely 5 minutes elapsed between injection and complete surgical anesthesia. Patient had previously been operated on for appendicitis, and said that inhalation anesthesia could not be compared with rectal, the latter was so much more agreeable.

Case IV.—Mrs. X; age, 40 years. Two-sided empyema. Operation by Dr. Freudenthal, by the Dencker method. Patient was informed that an injection would be necessary in preparation for the operation. The ether-oil solution was administered in a large ward. Anesthesia followed in 10 minutes, and the patient was removed to the operating-room. She vomited slightly at the beginning of the operation, which seldom occurs with this method, but otherwise she slept quietly during the entire operation. On awakening, 1 1-2 hours later, the patient could hardly realize that it was all over.

Case V.—Girl; age, 23 years. Chronic frontal sinusitis. Patient very timid. An hour before operation she was given morphin and atropin; 1 1-2 hour later chloretone (0.3g), followed in 7 minutes by the ether-oil mixture. Anesthesia was complete in 14 minutes. Slight cyanosis set in. About 2, ounces of the mixture was withdrawn, and thereafter the patient continued to breathe regularly. No postoperative nausea or distress of any kind.

Case VI.—A youth; age, 19 years. Deviated septum and enlarged tonsils. At 11:45 he was given a hypodermic of morphin and atropin, and at 12:15 a suppository of chloretone, 0.6g. At 12:45 the anesthetic began to take effect. Twelve minutes later the operation was begun and lasted 40 minutes. Immediately after the operation about 2 1-2 ounces excess ether was withdrawn from the colon, which was first sprayed with water, then with olive oil. The patient slept at least five hours. Then he vomited a little blood.

Note—The dosages in these 6 cases were not reported by Dr. Freudenthal.

FIVE OF DR. CANTLE'S RECENT CASES:

Case I.—Mrs. J. C., age, 63 years, weight, 160 pounds. Carcinoma of the left breast. Dosage 8 ounces of a 60 per cent. solution. Patient ready for operation in 22 minutes. Duration of operation, 1 hour and 25 minutes. Patient slept for 2 hours after operation. No nausea or vomiting. Patient had taken ether twice before but with this method had none of the disagreeable after-effects which had attended her previous operations.

Case II.—William K.; age, 9 years; weight, 74 pounds. Mastoid operation, left side. Patient very

septic at the time of operation with temperature, 103 degrees; pulse, 120; respiration, 28. Dosage, 4 ounces of a 50 per cent. solution. Patient ready for operation in 22 minutes. Duration of operation, 40 minutes. During first half hour of operation the pulse dropped to 110 and improved in quality and the patient was in much better condition when removed from the operating-room. He slept 20 minutes. No nausea or vomiting.

Case III.—Ella R.; age, 39 years; weight, 108 pounds. Necrosis of jaw. Dosage, 5 ounces of a 20 per cent. solution. Asleep in 20 minutes but not fully anesthetized for 35 minutes. Duration of operation, 20 minutes. Patient awakened on operating-table while bowel was being irrigated. Good recovery. No nausea or vomiting. Patient, due to a previous etherization had more fear of ether than of operation. She expressed herself as delighted with the ether-oil method and willing to be anesthetized in that way again, if necessary.

Case IV.—Eleanor S.; age, 17 months; weight, 23 pounds. Tubercular glands of neck. Patient very weak and emaciated. Dosage, 2 ounces of a 50 per cent. solution. Patient ready for operation in eighteen minutes. Duration of operation, 35 minutes. Patient slept for 40 minutes after operation. No nausea or vomiting.

Case V.—Robert J.; age, 27 years; weight, 180 pounds. Empyema, right side. Dosage, 9 ounces of a 60 per cent. solution. Patient ready for operation in 25 minutes. Duration of operation, 1-4 hour. Patient had a marked mitral murmur, but stood the operation well with no apparent change in the heart. Slept 2 hours after operation. Vomited once, shortly after awakening. About 1 ounce of mucous. No nausea.

CASE REPORTS OF DR. A. S. BRIKLEY—WITH COMPLETE URINALYSES.

The comparative clinical and microscopical appearance of the urine following the anesthetic, I have found to be about the same in both the inhalation and rectal methods of administration. I will give a short report of three cases:

Case I.—Mr. P. C, white, male, aged 28 years, Italian. Operated upon March 19, 1914. Operation, enucleation of glands. The patient was given 8 ounces of a 75 per cent. mixture of ether in olive oil. This was one of our first cases and no suppository of chloretone was given, and the patient complained of cramp-like pains in the rectum but not enough to expel the mixture. The mixture was allowed to run in slowly, about eight minutes being consumed. Two minutes later the patient was under full anesthesia. A radical dissection was done, lasting one hour and ten minutes with perfect anesthesia throughout. The patient returned to his room with pulse 100, and three hours later the pulse was 72. He vomited once three hours after operation. He had slight nausea that afternoon, but no nausea or vomiting afterwards. Highest pulse rate next day was 88 and temperature 99. Fourth day, the highest pulse rate was 80 and temperature 98. He had a very comfortable day and was given calomel on the third day. On the sixth day, the highest pulse rate was 78 and temperature 98; had a very good day. He has never complained of discomfort in the rectum. Patient left for home in good condition on the tenth day.

Urinalysis day before operation; color, amber, transparency, cloudy; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1020; microscopic examination, negative. First day after operation: color, amber; transparency, cloudy; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1025, and microscopic examination, negative. Third day after operation: color, amber; transparency, slight cloudiness; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1035, and microscopic examination negative. Sixth day after operation: color, amber; transparency, slight cloudiness; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1025, and microscopic examination, negative. A chloretone suppository was given to every one after this, and no further trouble with rectal cramps has been experienced.

Case II.—Mr. H. T., white, male, aged 19 years. Operated upon November 23, 1914. Operation, subtemporal decompression. Patient was given seven and one-half ounces of a 66 2-3 per cent. mixture of ether and olive oil preceded by a suppository of ten grains chloretone. The mixture was allowed to run in slowly, eight minutes being consumed, and *no discomfort was experienced*. The patient was quite a long time becoming relaxed, so after thirty minutes had passed ether by inhalation *was administered for one minute only*. The mask was removed and the patient remained under perfect anesthesia for the entire length of operation, which was forty-five minutes. The patient returned to his room with pulse 78 and respirations 18. Three hours later the pulse was 78 and temperature 98.4 and respirations 20. He vomited once nine hours after operation. There was no more nausea or vomiting. Highest pulse rate next day was 100. Patient was very restless and semi-delirious. He had been in this condition since entering the hospital. On the sixth day, pulse was 86 and temperature 98.4 and he was much quieter than usual. He left for home on the fourteenth day apparently much improved. He never complained of discomfort in the rectum.

Urinalysis day before operation: color, straw transparency, cloudy; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1022; diacetic acid, negative; microscopic examination, few pus and blood cells. The first day after operation: color, straw; transparency, cloudy; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1012; diacetic acid, negative; and microscopic examination, few pus and blood cells and calcium oxalate crystals. Third day after operation: color, straw; transparency, cloudy; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1014; diacetic acid, negative; and microscopic examination, few pus and blood cells. Sixth day: color, straw; transparency, cloudy; reaction, acid; sugar, negative; albumen, negative; specific gravity, 1018; diacetic acid, negative; and microscpic examination, occasional pus and blood cells

Case III.—Mrs. H. A. R., white, female, age 42 years, housewife. Operated upon October 11, 1915. Operation, amputation of the left hreast. This patient had taken anesthetic by open method before, and she had a great deal of apprehension and fear about taking it again. Sixty-six and two-thirds per cent. ether and olive oil was given, preceded by chloretone suppository—grains ten. Mixture was introduced slowly, ten minutes being consumed. The patient was under surgical anesthesia in eighteen minutes. A tumor-like mass was removed and frozen section made confirmed diagnosis of fibro-cyst adenoma. The operation was completed, including examination of frozen section, in forty minutes with perfect anesethesia throughout. The patient returned to her room with pulse 84 and respirations 20. Three hours later her pulse was 72 and respirations 20. She was slightly nauseated and vomited three times during the first six hours, but had no nausea or vomiting afterwards. Highest pulse rate next day was 90, temperature 99, and she had a very comfortable day. Fourth day she was given calomel. Her pulse was 74 and temperature 98.6. She was a little

uncomfortable from the calomel. Sixth day, pulse was 70, temperature, 98, and she had a very comfortable day. She never complained of any discomfort in the rectum. She left for home on the 12th day in good condition.

Urinaylsis day before operation: color, amber; transparency, clear; reaction, acid; sugar, negative; albumen, faint trace; specific gravity, 1020; diacetic acid, negative; and microscopic examination, few blood cells and calcium oxalate crystals. First day after operation: color, amber; transparency, clear; reaction, acid; sugar, negative; albumen, faint trace; specific gravity, 1024; acetone, very faint trace; and microscopical examination, one or two hyalin casts, few blood cells, and vaginal epithelium. Fourth day: color, amber; transparency, cloudy; reaction, acid; sugar, negative; albumen, very faint trace; acetone, negative; microscopical examination, few blood cells.

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PERFECTED METHODS OF ETHERIZATION . THE MILLER CLOSED CONE METHOD . PRELIMINARY MEDICATION . OIL OF ORANGE . ETHYL CHLORID . FERGUSON AND OPEN ETHER . THE ETHEROMETER . RICE'S SEMI-OPEN INTRAPHARYNGEAL AND CLOSED REBREATHING METHODS . ORAL AND NASAL VAPOR ANESTHESIA . CONCLUSIONS

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IN DISCUSSING PERFECTED methods of etherization it is important to consider several technics of anesthesia, popularized by constant usage, although they have been persistently misused. For instance the *closed cone method* of etherization had had the sanction of years of usage, but it has remained for A. H. Miller, of Providence, R. I., to establish the technic on a phsiological basis of the proper principles of vaporization, rebreathing and dosage. As a number of operators still persist in the demand that internes and anesthetists accommodate themselves to the closed cone method, it seems advisable to give a detailed explanation of the Miller technic, so that if the method continues to be used as a routine, it will henceforth be handled properly with the least distress and greatest safety to the patients involved.

THE MILLER CLOSED CONE METHOD OF ETHERIZATION

The Miller apparatus consists of an open cone which has an evaporating chamber at one end and a graduated glass syringe. A fresh cone is used for each case to insure rigid asepsis. It is manifestly unfair to the patient to use an inhaler previously contaminated by a case of tuberculosis, syphilis, or any other infectuous disease. The cone is a funnel open at both ends, made from pasteboard or paper and covered with a clean towel. It may be made from three sheets of newspaper folded to form a flat strip six inches wide. This is folded to form a funnel six inches long with a breadth of six inches when flattened out. This funnel having been neatly covered with a sterile towel, a diaphragm composed of eight layers of No. 1 surgical gauze, four by six inches, is placed over one end of the funnel. A strip of 38-1000 sheet brass, nickle plated, two inches wide and fifteen inches long, is bent to form a ring, which by means of clamps is adjustable in size. This ring is sterilized by boiling. It is placed above the gauze diaphragm and pushed into the funnel to the full depth of the ring, thus securing the diaphragm securely in position. There is thus formed a chamber, its sides consisting of the metal ring, its floor formed of the diaphragm of eight layers of gauze and its roof free. A handkerchief of No. 1 gauze, fourteen by thirty-six inches is shaken out and tightly placed in this chamber. The evaporating chamber is separated from the patient's face by an air space four inches deep. This air space provides a fractional amount of rebreathing, sufficient to vaporize the ether readily, conserve the carbon dioxid tension and insure an unchilled atmosphere. The glass syringe used for administering the ether has asbestos packing and is provided with convenient handles and a curved tip. The capacity of the syringe is one ounce or thirty cc. and it is graduated in half drachms. (Figures 1 and 2).

ADMINISTRATION.—Miller, preferably administers the anesthetic in the operating room or on the operating table, so that the patient does not have to be moved after anesthesia has begun. Quiet is strictly observed and no loud noises or conversation allowed. Preparation of the field of operation during the period of induction is not permitted. The patient is placed in a comfortable position, well covered with one or two pillows under the head. The

face is slightly turned to one side or the other. No surcingle or other restraining apparatus is used. An assistant stands ready to restrain the patient's hands if necessary. Also the eyes are not covered.

The gauze handkerchief is drawn partly out of the upper chamber of the funnel, leaving a clear airway at one end. A few drops of oil of orange are applied and then the cone is fitted closely to the patient's face, including the chin and bridge of the nose. (A sliding brass ring renders the cone adustable to any sized face).

Ether is now applied to the gauze handkerchief in small amounts until the patient becomes accustomed to breathing the dilute vapor

Figure 1. Showing the Miller cone; the gauze diaphragm about to be put in place.

and the olfactory reflexes have been fully obtunded. The graduated syringe enables the anesthetist to deliver minimal amounts of ether before pushing the induction. Once an acceptance of the ether vapor has been secured, the gauze handkerchief is pushed back into the chamber so as to fill it lightly but completely, and ether is added until anesthesia is complete. Half-drachm doses suffice. Each ounce of ether used is indicated on the chart as it is drawn into the syringe. The cone is not removed from the face except in the presence of some untoward complication. The temperature in the cone at an operating room temperature of 76° F. varies from 84° to 90° F., depending on the amount of ether which is being vaporized.

In this connection it is worth remembering that a can of ether containing 8 ounces by weight, having a specific gravity of .716, measures 11.17 ounces by volume. Ether boils at 96° F and becomes a vapor which is 2.586 times heavier than air. At lower temperatures it evaporates more slowly, the rate of vaporization at atmospheric pressure varying *directly* (1) as the temperature of the liquid ether, (2) as the extent of the evaporating surface, (3) as the rate of the renewal of the atmo-

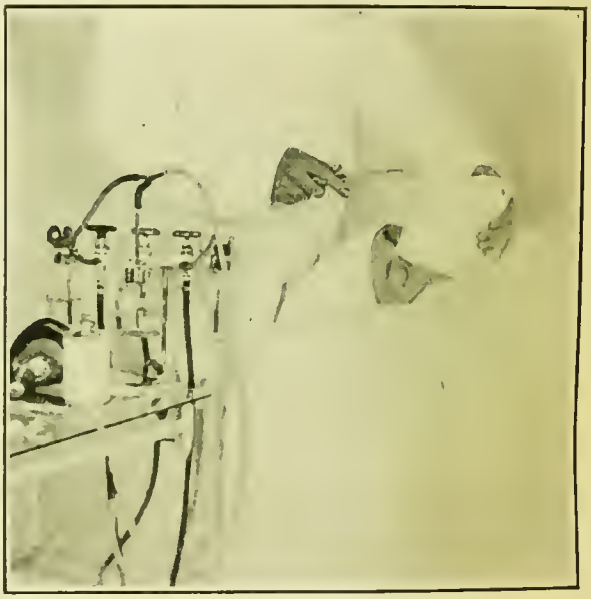


Figure 2. Showing method of nitrous oxid-oxygen preliminary to etherization. Cone in use and ether being added by means of the graduated glass syringe.

sphere and *inversely* (4) according to the amount of the ether vapor already in the atmosphere.

The vapor has practically the same temperature as the liquid ether from which it is given off. As ether absorbs heat when changing from the liquid condition to a vapor, the liquid ether and the vapor constantly become colder and the rate of evaporation is constantly diminished, unless heat, in some manner, is supplied to replace that lost.

To produce and maintain surgical anesthesia it is necessary to provide an atmosphere con-

taining from 15 to 30 per cent. by weight of ether vapor. The ether vapor displaces a corresponding amount of the atmospheric air. In producing ether anesthesia it is essential that the supply of atmospheric air be interfered with as little as possible, and that no mechanical obstruction with respiration be allowed. Cold ether is much more irritating to the respiratory passages than the same ether when warmed. One readily inhales a concentrated ether vapor at 95°F. while the same vapor at 45°F. is irrespirable by one who is conscious; and to use it for any length of time in the unconscious patient is to invite disaster. The temperature under the mask in the unimproved drop methods varies from 41° to 68°F., accounting for the profuse secretion of mucous during anesthesia and lung complications and toxemic symptoms postoperatively.

Open nitrous oxid-ether is the most satisfactory method of routine induction for the closed cone method in private practice. The cone and syringe are prepared as for the administration of ether alone. The gas inhaler is fitted to the patient's face and several inhalations of air are first allowed through the air-valve of the face piece. The gas is then admitted and at the first sign of anesthesia the inhaler is removed and the cone, impregnated with a drachm of ether substituted. Ether is administered rapidly enough to secure complete anesthesia in from two to five minutes and then more slowly throughout the operation.

The amount of ether used by this closed cone method of administration is indicated in several of Miller's personal charts, in which the amount of ether used during induction is included. This method is simple, clean and available for 80 per cent. of routine operations. The dosage of ether is measured, the tension of the vapor within the limitations established by Connell and Boothby, it is warmed by rebreathing, which also conserves the carbon dioxid tension, the induction can be accomplished with minimum discomfort to the patient and the after effects are negligible.

There is no longer any excuse for retaining the older technic of the closed cone method of administration with its constant overdosage, its cold vapor, smothering induction and postoperative nausea, vomiting and ether toxemia.

PRELIMINARY MEDICATION

Before proceeding to the consideration of open, semi-open and closed rebreathing methods of etherization, it seems advisable to briefly discuss the question of preliminary medication.

The hypodermic injection of a combination of scopolamin or hyoscin and morphin, is in the nature of a reversion to the narcotic methods of preanesthetic days, when a variety of potent drugs were used to stupify the patient. Given in relatively small doses the combinations of scopolamin or hyoscin and morphin are hypnotic, analgesic and anesthetic to the extent that operations may be performed with much smaller amounts of inhalation anesthesia, but in larger dosage the combinations may prove dangerous or even fatal.

My personal experience in alkaloidal premedication has been a most happy one. I first reported 105 cases with this preliminary medication in 1906 and during the past ten years have constantly used it in all cases in which the use of these drugs was not positively contraindicated.

Adult patients receive an average dose of scopolamin or hyoscin 1-1000 gr. and morphin 1-6 gr.; children, unless they are very young, proportionate doses. At times certain patients may present symptoms indicating that respiration is embarrassed, but never to an alarming degree. A hypodermic of atropin 1-150 gr. will at once stimulate respiration and obviate the occurrence of any untoward complication. During the past year I have added atropin 1-150 gr. to the combination of scopolamin or hyoscin and morphin and the new combination of alkaloids seems to be the best possible preliminary medication before the use of ethyl chlorid, ether or nitrous oxid.

Bevan, Herb and Ferguson are all more or less opposed to preliminary medication; Ferguson claiming that the use of opiates is not ordinarily desirable because it modifies two very important signs of the plane of anesthesia, the pupillary reflex and the character of respiration. The pupillary reflex is not of great importance, especially to the expert anesthetist and the addition of atropin to the combination of alkaloids obviates their depressing effects on respiration. Ferguson uses

the preliminary opiate in only three classes of cases: (1) patients with exopthalmic goitre, to provide for a tranquil state of mind and obviate the fear, which in some patients may lead to death before they reach the operating room; (2) inebriates, the pugnacity of alcoholism being replaced by the tranquility of morphinism, and (3) strong, robust young men of from 14 to 22 years of age who are apt to secrete a thick, tenacious mucous, which by obstructing the bronchioles and alveoli may prevent the ether vapor from entering the blood and producing anesthesia. This secretion is prevented by the preliminary use of morphin and atropin.

THE USE OF OIL OF ORANGE

In open and semi-open methods of etherization a valuable preliminary procedure from an esthetic standpoint is the use of oil of orange. The odor of this oil is at least twenty times stronger than that of ether and several drops on the mask will satisfy the olfactory sensibilities of the most fastidious patient. Providing the ether is not dropped too fast or the vapor too hurriedly administered, the oil of orange will entirely mask the odor of ether and will neither diminish the potency of the anesthetic or modify narcosis. The American essences do not answer the purpose as well as the oil because they are not nearly so strong.

After a proper interval from the injection of the preliminary medication, the patient is brought to the anesthetic room and placed in a comfortable position on the operating table with the assurance that conditions are entirely favorable for a safe anesthetic and a successful operation. (See R. A. Ferguson: Some Psychic Factors of Surgical Anesthesia: herewith printed in the Year-Book). While some object to it, I personally prefer the use of the eye pad, made of several layers of gauze and an adhesive strap to hold it in place. If patients are told that it is for the protection of their eyes, few will resent its use or complain of the smothering sensation alluded to by Ferguson.

THE PRELIMINARY USE OF ETHYL CHLORID

With these preliminaries briefly touched upon, we can now advance to a consideration of the use of ether chlorid to facilitate the induction of etherization. (For a general consideration of the subject of Ethyl Chlorid Anesthesia, I refer the reader to my paper presented during the Organization Meeting of the Interstate Association of Anesthetists in Cincinnati, O., May 4, 5, 1915, and shortly to be published in the Transactions of that Association in the Anesthesia Supplement of the American Journal of Surgery).

My present desire and intention is to deal with ethyl chlorid as a preliminary to etherization by various technics of administration. A few remarks on the physio-pathological properties of this anesthetic agent are imperative. The rapidity of its action has made the scientific study of this valuable anesthetic difficult and dangerous. It seems, however to affect the respiratory system more in a pathological than physiological way, (Muller). Patients sometimes have convulsive movements supervene during its administration and Hewitt has noted stertor, difficult respiration, tremors, tonic or clonic spasms of the extremities and masseters as untoward complications. In my personal experience with ethyl chlorid I have noted all these unpleasant symptoms, *but have found them to disappear almost, if not entirely under the concommitant use of oxygen.* Ethyl chlorid should never be given, except as a preliminary to etherization or for the briefest of anesthesias, without the concomitant use of oxygen. When so used even for protracted administrations, untoward complications rarely present, except in an occasional neurotic or hysterical patient, who may complain of a strangling sensation. In the presence of certain complications it is advisable to use oxygen with ethyl chlorid even as a preliminary to etherization, just as Gatch has indicated the advantages in extra hazardous risks of preliminary oxygenation preceding the administration of nitrous oxid and oxygen, to be later supplemented with ether.

Many of the difficulties of ethyl chlorid anesthesia are undoubtedly connected with the complications inherent to closed methods of administration and overdosing.

Ethyl chlorid as a preliminary to etherization may be conducted by the drop or spray methods. A graduated 3 cc. glass attachment has been perfected for attachment to the Gebauer container, which enables the anes-

thetist to use the drop method of induction and as the anesthesia deepens to also spray the anesthetic agent. Other containers have automatic spray attachments and calibrated tubes by means of which the approximate dosage used may be readily established. Some anesthetists prefer ampoules. Whichever containers are used the technic of administration is practically the same.

Ethyl chlorid is either dropped or sprayed on the gauze of the vaporizing chamber of the inhaler, in minimal amounts, until the nasal reflexes have been obtunded. After a few inspirations the drop or spray is increased and when the patient's respirations become deeper and rhythmical, ether is preferably added synchronously with the continuation of the ethyl chlorid until positive signs of ether anesthesia present. This stage of preliminary anesthesia last from one-half to one minute or more in different subjects, (the obese and alcoholic) and from 3 to 9 cc. of ethyl chlorid may be required, depending considerably on whether open, semi-open or closed-rebreathing methods are used and whether the ether is used synchronously before the ethyl chlorid is discontinued. If this transition is expertly done and neither the ethyl chlorid or ether are crowded until consciousness has been lost and reflexes abolished, then the induction of etherization can be accomplished without any noticeable stage of excitement or the least discomfort to the patient. Should the patient show signs of incomplete anesthesia after the withdrawal of the ethyl chlorid, there is no contraindication to its resumption, although in such instances a minimal amount will usually suffice to establish surgical narcosis in conjunction with the ether. The application of ethyl chlorid as a preliminary to etherization will be further discussed in the consideration of the several open, semi-open and closed, rebreathing methods that will be explained in detail.

THE OPEN DROP METHOD OF ETHERIZATION

The so-called open drop method of etherization was originated in 1893 by Dr. Lawrence H. Prince. It was hoped that the method which so readily furnished the approximate 2 per cent. vapor for chloroform anesthesia woud answer equally well for the 15 to 30 per cent. vapor required for etherization, but the analogy did not hold good. The open drop method was then modified and popularized in the Mayo Clinic by limiting the free supply of air by wrapping a streamer of gauze about the mask and confining the evaporating surface in this or some similar method. Theoretically a constant succession of drops of ether falls on the evaporating surface and each drop immediately is vaporized. In practice the evaporating surface soon becomes chilled by the loss of heat from evaporation and the drops of ether are not immediately vaporized but may so soak the evaporating surface that it no longer allows the unimpeded passage of air. This consideration led Ferguson to attack the problems underlying the open drop method of etherization and he established it on a basis of routine success.

Ferguson's definition of open ether anesthesia is: *One in which the respiratory gases have an unrestricted interchange between the patient's lungs and the external air, at the same time that the ether vapor is inhaled in sufficient amount to produce and maintain adequate surgical anesthesia.. Hence an open ether anesthesia is conducted by apparatus, the purpose of which must not extend beyond the holding of the liquid ether while it evaporates and the conserving of the vapor for the patient's use. Neither the ether vapor nor the exhaled air must be confined in such quantities or for so long a time that the confinement itself can exercise any appreciable influence on the anesthesia.*

Ferguson's inhaler, adopted later by Luke of Edinburgh, and improved by McMechan, is essentially a double chamber mask with a face-piece made of flexible wire to conform to the shape of different faces. The face-piece is covered with 8 or 10 layers of wide mesh surgical gauze, which are clamped into position by a spring. The superstructure is covered with a flanelette cover, having a drop hole above or on either side of the inhaler, depending on the type of operation for which anesthesia is administered. Ferguson conducts his entire etherization with ether alone.

McMechan's improvement of the Ferguson inhaler is a combination of the Yankauer face-piece with a more rigid superstructure, patterned after that of Ferguson. The double

chamber principle is identical. The flanelette cover has three drop holes, two of which are closed while the required one is used. The face-piece has a nipple and perforated rim for concomitant oxygenation. McMechan uses the drop method of ethyl chlorid as a preliminary dropping from 1 to 2 cc. until rhythmical breathing occurs, at which time ether by the drop method is added synchronously and both

or nascent oxygen from an Autogenor is used for concomitant oxygenation in the presence of respiratory embarrassment or acute toxemia; and postoperatively oxygen is used with a fresh mask by the rebreathing method devised by Gatch for gas-oxygen-ether, for clearing the remnants of the anesthetic fumes from the alveoli and tissues.

In the open drop method of etherization

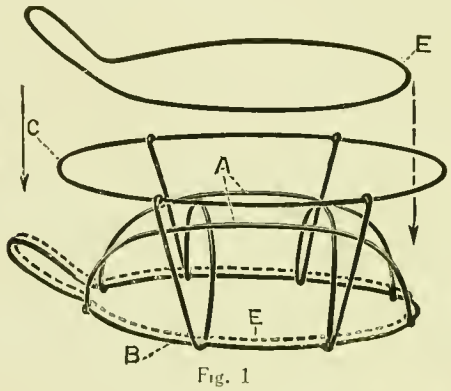


Fig. 1

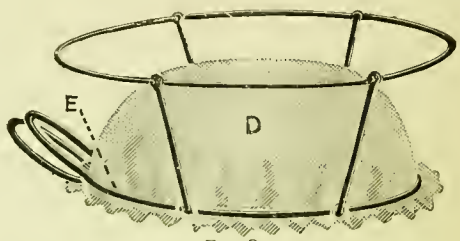
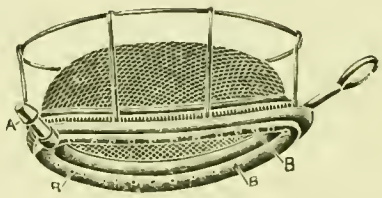


Fig. 2



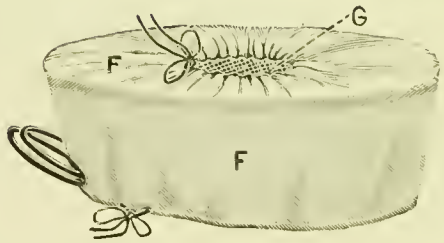


Fig. 3

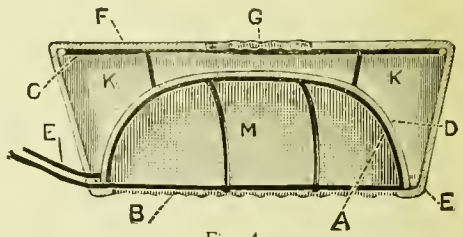


Fig. 4

Figure 3. (Figs. 1, 2, 3, 4) The Ferguson double chamber mask for etherization by the open drop method. The manner of preparing the mask is indicated in detail. (5) The modified McMechan mask with attachment for concomitant oxygenation.

agents are continued until positive signs of ether anesthesia present. Occasionally from 6 to 9 cc. of ethyl chlorid may be required in recalcitant subjects, but usually 3 cc. suffice. For anesthetizing alcoholics McMechan prefers a C_2E_5 Mixture, preceded by ethyl chlorid for the induction with the use of ether alone after surgical anesthesia has been fully established. Oxygen from a low pressure tank

Ferguson uses a grooved cork with a gauze wick extending to the bottom of the ether container as a dropper; McMechan employs either a glass-bottle dropper or the new Grommet dropper directly attached to the can. Varying quantities of ether are required for induction, but the dropping must never be so rapid as to induce reflexes during induction or to soak the gauze over the vaporizing chamber.

Once anesthesia has been established from 2 to 3 drops per respiratory movement usually suffices in adult subjects to maintain a satisfactory plane of surgical narcosis without im-

Figure 4. Grommet dropper attached to ether container.

periling muscular relaxation. In hazardous risk concomitant oxygenation, about 100 bubbles per minute, will add materially to the safety of the anesthesia and also go far in obviating postanesthetic sequelae.

The investigations of Hewitt, Legg and Symes have proven that about 8 layers of surgical gauze over the vaporizing chamber in the drop method permits the establishment of ether percentage vapors varying between 6 and 22, well within the limitations set by Connell and Boothby. If the dropping of the ether is expertly done a percentage vapor of about 12 to 15 may be readily maintained throughout anesthesia. This is all the more readily accomplished with a double chamber mask, as the slight amount of retention and rebreathing provides sufficient heat to vaporize the ether dropped, almost immediately, conserves the requisite carbon dioxid tension, thus preventing overventilation, and also enables the anesthetist to keep the patient's color pink, a positive indication that he is not precipitating an acidosis.

THE ETHEROMETER METHOD OF ETHERIZATION

The dropping of the ether in the open method is an annoyance to some anesthetists and the Etherometer disposes of this inconvenience. By means of this automatic device, I believe, the anesthetist is enabled to accomplish the easiest, safest, most efficient and satisfactory open etherization. The Etherometer consists of (a) a mask resembling the Yan-

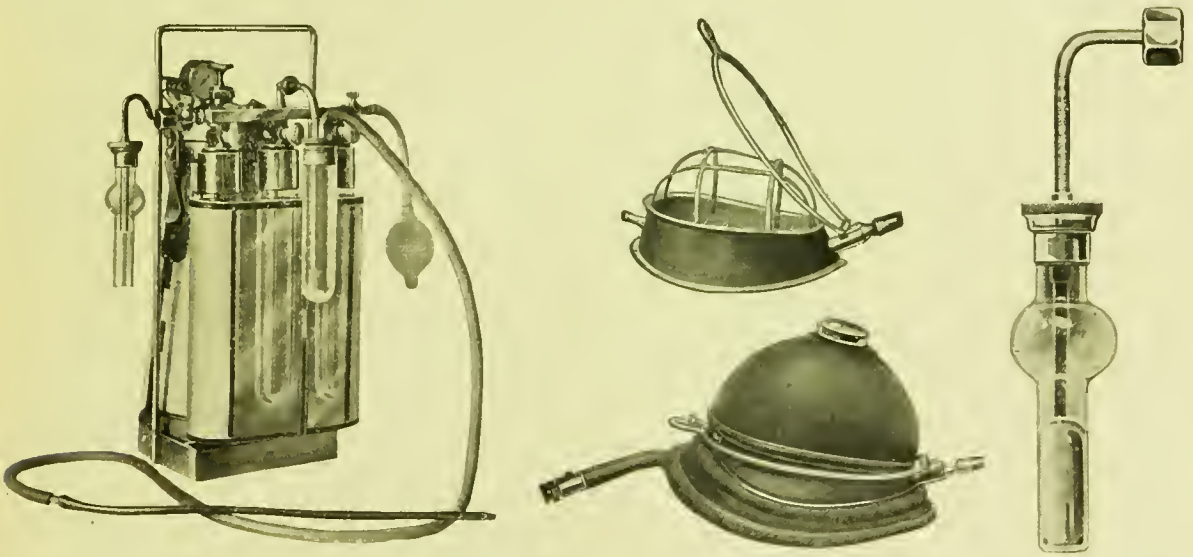


Figure 5. The Autogenor for the Vapor method of etherization. Nascent oxygen passes through the ether container and is delivered to the mask, (which is arranged for drop ethyl chlorid-ether induction) or to the mouth-gag or intrapharygeal or intratracheal tubes. A mercury manometer, adjustable to varying millemetric pressures is provided for intratracheal insufflation.

kauer face-piece and (*b*) a graduated glass bottle holding eight ounces of ether. The capillary metal tube (c) connects the mask and ether container at (d) just above the bridge of the nose, which point the capillary tubes run up on the mask's wire mesh, which is covered with 12 layers of wide mesh surgical gauze, held in place by the usual spring. Any number of ounces of ether up to eight may be put in the container and the top (e) screwed on. Air is pumped into the container by means of the rubber bulb (f); a regulator (g) controls the frequency of the drops projected into the small glass dome (h) from which the ether is transferred by the capillary tube to the evaporating surface of the mask. A clamp (i) holds the ether container firmly fixed to the operating table, irrespective of its position, (Figure 6).

For the anesthetist prejudiced against the open drop method of etherization, the advantages of this device are many. The mechanical dropper gives a much more even anesthesia than when the dropping is done by hand with the makeshift wicks and droppers, while both hands of the anesthetist are practically free at all times to attend to the patient and handle any emergency demands. Etherization by the Etherometer may be preceded by oil of orange and ethyl chlorid. A few drops of the former are placed on the mask and the odor inhaled until the olfactory reflexes are saturated; then ethyl chlorid is dropped or sprayed on the evaporating surface of the mask until rythmical breathing supervenes, at which time the

Figure 6. The Etherometer in use.

Figure 7. The Rice Inhaler for semi-open methods of etherization.

flow of ether is started and the two agents continued synchronously until ether anesthesia is fully established. When ethyl chlorid is used oil of orange is not essential as few patients object to the odor of ethyl chlorid and consciousness is so rapidly lost that patients have little or no opportunity to notice its effects.

Personally I am not partial to the open drop method of etherization as routinely conducted. I prefer a method in which not so much of the vaporized ether is blown out into the operating room. This ether vapor is really meant for the patient to respire not for the anesthetist, surgeon and nurses; hence a semi-open method, in which the anesthetic vapor is conserved, is preferable. This may be and has been accomplished in many different ways, as by encircling the mask with a streamer of gauze, by covering the face and mask with towels, wet or dry, by covering the gauze on the wire mesh of the vaporizing chamber with a rubber dam, or by means of a suitable chamber above the evaporating surface. All these methods, however, change what is the so-called open into a semi-open method of anesthesia. Undoubtedly these various means for conserving the ether vapor enable the anesthetist to produce a sufficiently profound anesthesia for any operative procedure, but I cannot agree with Ferguson that a trustworthy anesthesia can be obtained for all cases by the strictly open method. Ferguson claims that the efficiency of the open drop method of etherization is illustrated by the fact that probably 90 per cent. of all routine anesthesias are now conducted by this method. I think the only difference

Figure 8. The improved Lumbard mask for vapor anesthesia.

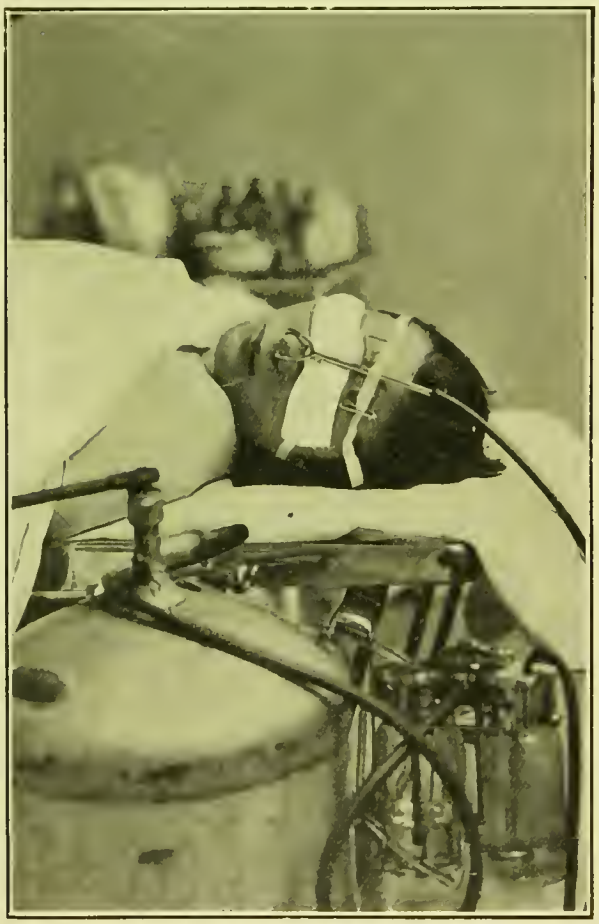


Figure 9. Adjustment of the nasal tubes for intrapharyngeal anesthesia by the vapor method.

between Ferguson and myself is as to what constitutes an open anesthesia. If he considers his own inhaler or the McMechan improvement as an open drop ether method of anesthesia, then I agree with him that the method is not only efficient but that practically 90 per cent. of all anesthesias are conducted as open etherizations. In reality, however, this double chamber mask is a semi-open method, since it not only conserves the ether vapor, but also the nesessary degree of carbon dioxid retention to maintain muscular and venous tone.

RICE'S METHOD OF SEMI-OPEN ETHERIZATION

My own method for the past eight years, in all cases, except tonsil and adenoid and other operations in which a mask would interfere with the operative procedure, has been the semi-open with an inhaler of my own design. It is practically an open drop method changed to a semi-open method by a superimposed chamber over the vaporizing surface to conserve the ether vapor, (Figure 7). This inhaler consists of (a) an oval metal face-piece adaptable to varying faces by an inflated rubber cushion. From the inner edge of this oval face-piece a wire mesh extends nearly half as high as the outside of the lower half of the inhaler. Over this wire mesh are placed eight layers of surgical gauze, this number having proven the most satisfactory. On the side opposite that shown in the illustration is a petcock connection, through which a rubber tube

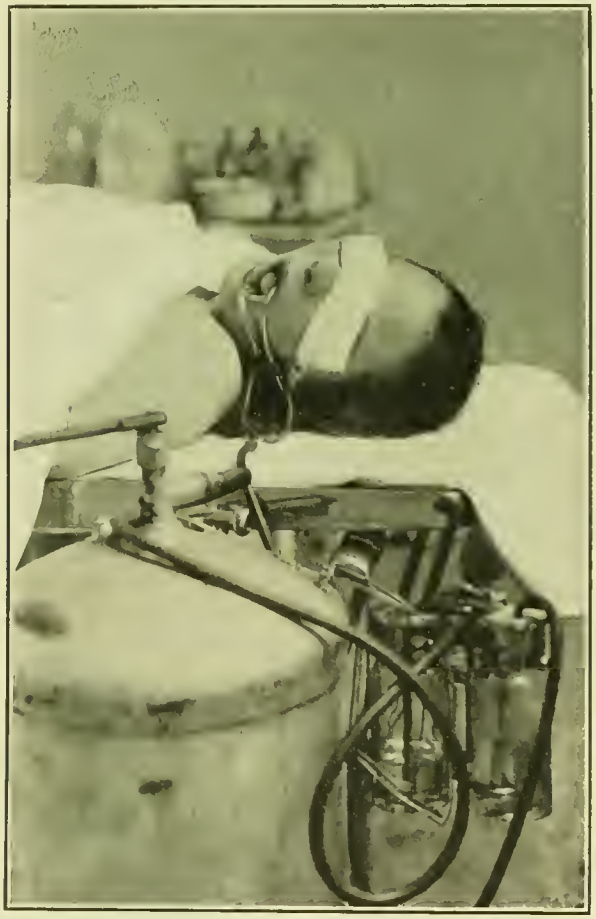


Figure 10. Adjustment of mouth-gag for vapor anesthesia for tonsil and adenoid operations.

Figure 11. Rice's latest apparatus for the closed-rebreathing vapor method of etherization with concomitant oxygenation.

(b) from the Gwathmey three bottle vaporizer delivers oxygen, when the patient usually a short-necked individual, needs it to produce relaxation. In the top of the superimposed chamber and on each side are valves (c) the top one being used especially for delivering ethyl chlorid as a preliminary. This top valve and at least one of the side valves are usually left open after the ether is started, because a certain amount of fresh air must enter the upper chamber over the gauze to vaporize the ether more readily. If all these valves are closed the patient does not stay well relaxed as the vaporization is too slow and there is too much retention of carbon dioxid, with its consequent stimulation.

In inducing etherization by this method, ether is dropped on the gauze of the vaporizing chamber just as fast or as slowly as the individual case may demand, from the ether container (d) regulated by the thumb screw (e). While part of the ether vapor is blown out through the open valves most of it is conserved for rebreathing. This limited amount of rebreathing warms the vapor practically to body temperature and is far warmer than the vapor inhaled in the ordinary open ether methods. Should the Trendelenburg posture be required, the ether dropper can be rotated by moving the oval (f) on which the dropper is secured, so that it can be kept in a vertical position, no matter how the patient's position is altered. The opening (g) is an expiratory valve. When the inhaler is used for the semi-open method this valve is of no especial value, but it is necessary when the rebreathing attachment is used. This inhaler should be used when the semi-open drop method is desired. If the closed method is preferred, the ether should be vaporized by passing oxygen through it, before the vapor is admitted to the mask.

Another excellent apparatus (Figure 9) consists of a mask similar to that used in connection with the Etherometer. It is my improvement of the Lumbard mask. The wire mesh has been soldered up to prevent the loss of vapor, and an expiratory valve (b) has been set just in front of the hose connection (c) for the entrance of the vapor. To prevent dilution of air between the face-piece and the face of the patient, an inflated rubber cushion is used. This inhaler for the ether-oxygen vapor method is very satisfactory and decidedly economical as the only ether vapor that is lost is the small amount that passes out of the valve with each expiration.

THE INTRAPHARYNGEAL METHOD OF ETHERIZATION

The intrapharyngeal method of etherization is a method that is coming more and more into routine use and is of very great convenience to the operator in certain operative procedures, (Figure 9). In using this method it is essential to induce a surgical plane of anesthesia by the semi-open method of etherization, after which the transition to the intrapharyngeal method may be made. An inadequate degree of preliminary anesthesia will imperil a smooth transition. When the proper plane of anesthesia has been induced the intrapharyngeal tubes are introduced. These tubes are preferably of soft rubber, about five inches in length, the diameter varying according to the nares of the patients operated on. These tubes are introduced into the anterior nares and pushed into position in the nasopharynx. They are connected to a metal nose piece, which in turn is held in place by an adhesive strap across the patient's fore head. Ether vapor is supplied by passing oxygen, under low pressure, through a Gwathmey three bottle vapor apparatus. This apparatus consists of an ether, chloroform and hot water bottle, with a regulating valve, enabling the anesthetist to use ascending and descending, proportionate, percentage of vapors of ether or chloroform alone or in the combined C. E. mixture. In all procedures in which the airway is at all obstructed or hemorrhage that may embarrass respiration is expected, it is advisable to use oxygen for producing the vapor rather than atmospheric air. The nitrogen percentage of atmospheric air prevents the patient with impeded respiration from being properly oxygenated and from receiving, at the same time, an adequate amount of ether vapor. Packing up the pharynx may be used to control hemorrhage and insufflation of blood into the trachea, but a good suction apparatus, properly applied at intervals or continuously, when necessary, is far more efficient. The intrapharyngeal method of etherization is the method of choice in all operations about the face and in the

mouth and throat, except tonsil and adenoid operations.

For this latter procedure the vapor is preferably administered through a mouth-gag provided with anesthetic tubes. The patient is brought to a surgical plane of anesthesia before the gag is introduced and adjusted in such a manner that the extent to which it is opened does not interfere with respiration. This is important, because occasionally one more notch on the ratchet may embarrass respiration. The anesthetic tubes of the gag are united in a Y connection by means of rubber tubes and then connected with the vapor apparatus. In operations of this character, with the nose and mouth wide open, there seems no especial reason for the use of oxygen, as the dilution of atmospheric air may render it difficult to secure a sufficiently strong ether vapor to maintain ether anesthesia. If the C. E. mixture is used, oxygen is desirable as a prophylactic against the effects of chloroform, should respiration become embarassed from hemorrhage or the manipulations of the operative procedure. Also in the presence of even mild grades of cyanosis, oxygen is advisable as the vehicle for the ether vapor. A constant stream of vapor must be supplied, if an even plan of anesthesia is to be maintained. Occasionally it may be necessary to pinch the nose for a few moments or cover the open mouth of the patient with one's hand to deepen anesthesia or change nasal to oral or oral to nasal respiration.

Of all the apparatus personally used, the Gwathmey device has proven itself the most satisfactory for vapor anesthesia. I prefer the use of ether alone, unless it is impossible to control certain types of recalcitrant patients without the addition of chloroform. This C. E. mixture with a high dilution of atmospheric air or oxygen is undeniably safe and free from anesthetic dangers and postoperative complications. Used in connection with a low pressure tank of compressed air or oxygen, or the Autogenor, the Gwathmey device gives any desired regulation of the anesthetic mixture by a simple movement of the regulating valve and the flow of the vapor can be instantly controlled by the valve on the air or oxygen tank. Thus both hands of the anesthetist are practically free to assist the operator, keep the gag in position, aspirate blood or mucous, and meet any emergency demand that may arise. Once the surgical plane of narcosis has been fully established by semi-open etherization, the continuous flow of the vapor apparatus will suffice to maintain a perfectly tranquil form of anesthesia during which any operation on the face, nose, mouth or throat may be expeditiously performed.

THE CLOSED-REBREATHING METHOD OF ETHERIZATION

In an experience of 12 years as Chief Anesthetist to Grant Hospital, Columbus, O., during which time some 20,000 anesthesias have been administered, I have used ether, chloroform, ethyl chlorid, ethyl bromid and nitrous oxid and oxygen, alone or in combination or sequences. Experience and observation have not made me enthusiastic over strictly open etherization, and I have always preferred the semi-open or more or less closed methods.

Since the researches of Yandell Henderson and Levy on acapnia, I am more than ever convinced that the rebreathing method of ether is the ideal one. In May, 1915, I had a special apparatus made for my work and I think my expectations of what it would accomplish have been more than realized. The low pressure oxygen tank and the Gwathmey vapor apparatus are used in connection with the rebreathing apparatus, (Figure 11). The oxygen bubbling through the ether, (or in very exceptional cases through the ether and chloroform), forces the anesthetic vapor through a rubber tube to the pet-cock (a) on the bottom of the small chamber (b) to the end of which is attached the rubber breathing bag (c) and to the other end a metal Coburn breathing tube (d); just back of the chamber is a standard and forehead piece (e) resting the weight of the apparatus just above the brows. This steadies the tube, which is inserted to the base of the tongue, from moving in the pharynx and doing any possible injury to its walls. If the rebreathing bag becomes too distended, as it may in patients, with some forms of respiration, it may be emptied by turning the pet-cock (f) in the free end of the bag.

From a practical point of view this is an ideal method. It delivers an oxygenated ether vapor, evidently of correct tension and proportions, for all patients are easily kept asleep and

in a perfect respiratory and sufficiently relaxed condition. Many times I have had patients in whom it was extremely difficult to maintain a pink color, necessary for the proper degree of muscular relaxation by the open or semi-open methods, but the instant this apparatus was placed in position, they at once assumed a nice, pink color, with unimpeded, regular respiration and sufficient without imperiling muscular relaxation.

Extended experience with this closed, rebreathing vapor method, inclines me to the belief that practically all patients require the same ether tension in the inspired anesthetic vapor. By this I do not mean that the same amount of ether will suffice, for some patients of robust type will blow away much more of the vapor than weaker individuals. The same is true when methods other than the rebreathing are used. In the latter, however, no vapor need be lost at all. Both nostrils are plugged to insure oral respiration, and by this method the patient inspires nothing but pure oxygen and ether vapor. The color is always pink, the respiration regular, strong and unimpeded, the pulse slow and full, and the skin dry. My impression is that postoperative shock and distress is considerably less after procedures of equal length and severity, in comparison with the sequelae following other methods of etherization.

While the percentages of ether vapor used in some of the methods employed have not been experimentally determind, their efficiency without untoward complications, and their freedom from postanesthetic sequelae would practically establish them within the limitations set by Connell and Boothby.

It must be remembered that some patients require a much more concentrated vapor than others for preliminary saturation of the circulation with the proper tension of ether, but once this saturation has been accomplished, these patients apparently require little more than other individuals to maintain a satisfactory plane of anesthesia.

There are occasional patients whom it seems almost impossible to anesthetize to a successful degree with any method or tension of ether vapor alone. In these cases the additional, minimal amounts of chloroform required, may be used with perfect security, especially by the vapor method in connection with ether and concomitant oxygenation. In some of these patients even closed methods of etherization with rebreathing fail to establish satisfactory anesthesia, although the ether vapor is warmed. A few such cases present in the experience of almost all expert anesthetists who have written on the subject.

In practice it is difficult to establish definite amounts of the anesthetic agent or fixed percentages of its vapor, for inducing and maintaining anesthesia in individual cases. The whole conduct of anesthesia must be governed by the instinctive adustment of amounts and percentages which is borne of extended experience and careful observation of the signs of anesthesia or impending complications.

It is more difficult to administer a smooth anesthesia by the open or semi-open methods, when ether is dropped by hand. Mechanical control of the dropping or percentage adjustment of the vapor delivers to the patient a more constant tension in the inspired air than can be otherwise secured.

Ferguson and Miller both call attention to the influence of temperature, humidity, speed of dropping, rapidity of evaporation and character of respiration as factors complicating the open or semi-open methods of etherization, and these factors must be properly dealt with before the methods in which they are inherent are routinely successful.

While it is a truism, as Coburn states, that all anesthetics adminstered via the respiratory tract are administered as vapor, there may be considerable difference in the respirability and absorption of this vapor on account of the manner in which it is produced or delivered. In all methods there are mechanical limitations to the rapidity with which the anesthetic can be vaporized and the percentage tension in which it can be delivered and absorbed. Coburn, in his apparatus, mechanically drops the ether on gauze in a chamber, and uses a Politzer bag to provide the air current for delivering the ether vapor to the patient. Such an apparatus, undoubtedly is efficient, and provides an ether tension in the inspired air that will prove effective in the majority of cases, but by judicious regulation, the method seems to have no advantages over sending the air current directly through the ether container. This latter method requires an ether container of sufficient size to volatize an adequate amount

of vapor and a stream of air or oxygen broken up into a series of fine bubbles to take up the vaporized anesthetic. In this connection, Buxton's contention must be recalled, that concomitant oxygenation enables the circulation and tissues to absorb more of the anesthetic agent (ether) and establish a more profound anesthesia without the danger of imperiling complications.

In point of economy it may be mentioned that the several ounces of ether required for induction in the open and semi-open methods of etherization, will in the method of pharyngeal rebreathing, previously described, maintain anesthesia for almost an hour. Such an economical use of the anesthetic deserves consideration, not only from the mercenary standpoint, but also on account of its prophylactic influence in sparing patients from ether toxemia and its distressing complications.

Overdosage always results in acapnia, tissue saturation and excessive muscular relaxation and these in turn precipitate acidosis, lung complications and hypotension postoperatively.

CONCLUSIONS

In conclusion it may be again emphasized that perfected methods of etherization are primarily based on the administration of minimal amounts or percentage vapors of the anesthetic, compatible with surgical anesthesia, in a medium that will provide sufficient oxygenation for all vital requirements, while at the same time rebreathing conserves the carbon dioxid tension necessary to stimulate respiration and preserve muscle tone; secondarily an expert administrator is required to adjust these essential factors to the requirements, not only of individual patients and their pathological condition, but also to the exigencies of any operative procedure.

TO KNOW EVERY DETAIL, TO GAIN AN INSIGHT INTO EACH SECRET, TO LEARN EVERY METHOD, TO SECURE EVERY KIND OF SKILL, ARE THE PRIME NECESSITIES OF SUCCESS IN ANY ART, CRAFT OR TRADE. NO TIME IS TOO LONG, NO STUDY TOO HARD, NO DISCIPLINE TOO SEVERE FOR THE ATTAINMENT OF COMPLETE FAMILIARITY WITH ONE'S WORK, AND COMPETENT EASE AND SKILL IN THE DOING OF IT. AS A MAN VALUES HIS WORKING LIFE HE MUST BE WILLING TO PAY THE HIGHEST PRICE OF SUCCESS IN IT,—THE PRICE WHICH SEVERE TRAINING EXACTS.

—*Hamilton Wright Mabie.*

THE USE OF NITROUS OXID IN OBSTETRICS . HISTORICAL REVIEW . EFFECTS ON MOTHER AND BABE . TIME LIMIT OF ADMINISTRATION . EFFECTS ON THE PROGRESS OF LABOR . GENERAL DISCUSSION OF ANALGESIA . TYPES OF PATIENTS . COMBINED NARCOSIS . INCIDENCE OF LACERATIONS . PERINEAL INFILTRATION . NITROUS OXID AND OBSTETRIC OPERATIONS . POSSIBLE ACCIDENTS . COST OF ADMINISTRATION . TECHNIC . SELF-ADMINISTRATION . INDIVIDUAL PAIN APPLICATION . CONTINUOUS ANALGESIA . INTERMITTENT NARCOSIS . CONTINUOUS ANESTHESIA . REBREATHING . APPARATUS.

BY ARTHUR E. GUEDEL, M. D. *INDIANAPOLIS, INDIANA*

THE APPLICATION OF nitrous oxid in the field of obstetrics is a logical development. Women of today are justly demanding our best efforts toward diminishing the suffering of labor. There is necessity for more prolonged and greater relief than we can safely secure with chloroform or ether, and although morphin-scopolamin seminarcosis has been urgently advocated, it is evidently not the method we are seeking, as is manifest by the honest antagonism of a great and good part of the profession.

GENERAL CONSIDERATIONS

Any single anesthetic agent which will prove universally satisfactory in all cases of obstetrics probably never will be found. The necessary qualifications of such an agent, applied as our present-day obstetrics indicate, are many. It should have no ill effect, immediate or remote, upon either the mother or the babe. It should render true physical relief from suffering, and should be applicable over a long period of time without influence upon uterine contraction. It must present to the obstetrician a patient in satisfactory condition for correct delivery, and to be practical it must admit of convenient and simple application.

Of the various anesthetic agents now at our command nitrous oxid is probably the most nearly adapted to the fulfillment of these qualifications. My experience with nitrous oxid in labor since 1910, together with generally favorable reports of its application from various parts of the country during the past two years, afford security to the statement that its application in this work has come to stay.

HISTORICAL CONSIDERATIONS

A search of the literature discloses that nitrous oxid in obstetrics is by no means new. In 1878 it was recommended by Paul Bert. Following Bert's recommendation Klikowitsch (Petrograd) in 1880 reported 25 cases of labor in which he had used laughing gas with satisfactory results. Then followed reports by Tittle in 1883; Doederlein in 1886, and Hillischer in 1887. While no mention was made of analgesia in these reports, it is probable that these men were working under an imperfect analgesia or light narcosis, not recognizing the difference between the two states.

In Edgar's English edition of Winckle's textbook (1890) there is an interesting discussion relative to this work, in which many observations correspond to ours of today. Their imperfect results were probably due to the inadequate apparatus afforded by that period, as well as to insufficient knowledge of the state of analgesia as it is now understood.

Winckle states that: "Narcosis by means of laughing

gas is not dangerous and may be discontinued at the will of the parturient woman. It relieves the pain in proportion to the intelligence of the person, stupid persons often withstanding its influence for a long time before its favorable influence is felt. Women to whom it is not administered until the stage of expulsion can seldom be induced to inhale it quietly, while if it is administered in the first stage of labor its beneficial action is at once felt and extends to the second stage."

His next statement is illustrative of the crude apparatus employed at that time.

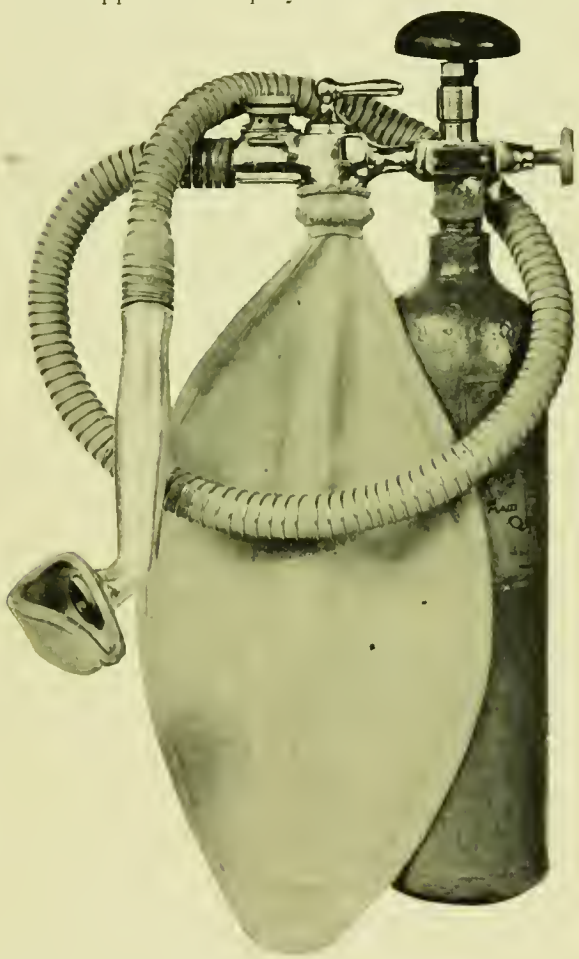


Figure 1. The Guedel apparatus for the self-administration method of analgesia in obstetrics.

"It seems most practical to get the gas from the apothecary, and that he should be provided with rubber bags which he may fill and furnish to the physician as needed. In this way the gas may be introduced into private practice and not monopolized by the clinics. The apparatus consists of a rubber bag like a pillow, is inconvenient it must be confessed, but this is entirely subordinate. In abnormal painful labor it is at any rate an extremely important remedy."

The remarkable feature of these earlier investigations is that nothing came of them. This is probably explained by the difficulty of securing the gas and an apparatus suitable for its application.

Sporadic cases are reported from that time on, but no general interest has been created until within the last few years, during which time it has been taken up by a number of men in this country either with or without knowledge of the work done by others. In almost all cases the operators using this method of analgesia have reported favorable results, and the majority are enthusiastic over their success.

During the past year obstetric analgesia with nitrous oxid has been inaugurated in a number of hospitals and appears to have been permanently adopted.

GENERAL RESULTS OF REPORTED CASES

I have collected reports of more than 1,800 cases. These come from all parts of the country from anesthetists and obstetricians, and represent cases conducted under all circumstances, both in the hospital and in the home. The early reports (1880-1886) are not included in this number.

When it is considered that these cases were conducted by many different men, with a majority of them during the past two years, the number of favorable results reported is remarkable. Favorable results are reported in 98.5 per cent. of the cases; the 1.5 per cent. unfavorable results representing cases in which the mother apparently did not secure sufficient relief from the gas. There are no reports of any more unfavorable results than this.

All sorts of technics were employed, and the combinations of gases show considerable variation. The period of time during which the gas was applied in these cases varied from one-half hour to 10 hours. More uniformly successful results were secured after the first few cases, which were reported more or less bungled.

These results, coming for the most part from beginners in the use of this method, are promising. The number of favorable results will probably not be increased by further study, but as the work progresses the standard of favorable results will no doubt be elevated.

THE GENERAL EFFECT ON MOTHER AND BABE

Nitrous oxid as it is applied in obstetrics has no apparent ill effect on either the mother or babe. Not being broken up into its component elements at body temperature, it accomplishes its purpose and is eliminated through the lungs as nitrous oxid unchanged. The most unpleasant effect that has been noticed as occurring with any recognizable degree of frequency is headache, usually mild and transitory. (See Rebreathing).

dependent in a secondary way upon the oxygen deprivation which the gas produces.

In analgesia, with the dose of nitrous oxid small, these phenomena are hardly noticeable except to a slight extent during the period of induction.

Mucous Membranes.—Under ordinary circumstances nitrous oxid produces no irritation of the respiratory mucous membranes. Under extraordinarily rapid and continous administration such irritation is possible, as the result of cold alone.

Figure 2. Showing the Guedel apparatus in use during the progress of labor

Circulation, Respiration and Blood Pressure.—Under ordinary circumstances the circulation and respiration are accelerated and the blood pressure increased about 5 to 10 millimetres. This stimulation is noted to a greater extent when the gas is administered in full dosage, to narcosis. Circulation and respiration are increased and blood pressure elevated, in equal proportion, dependent upon the rapidity of administration. This is not due primarily to the action of nitrous oxid, but is

Nitrous oxid is stored in liquid form, in metal cylinders, under pressure of a thousand pounds or more. When the cylinder valve is opened and this pressure relieved, the rapid conversion of the liquid into a gaseous state is attended with the production of extreme cold. The temperature of the gas in the supply bag is reduced in proportion to the rapidity of release of gas from the cylinder, and if the gas be administered rapidly and continuously for a period of several minutes there may occur a

slight irritation, by chilling the mucous membranes of the upper respiratory passages. I have observed considerable frost in the nares of patients, after 20 or more minutes of forced anesthesia with a nasal inhaler for operations within the mouth, but in these cases the resultant irritation did not extend into the nasopharynx.

As such administration is never practiced in obstetrics, it may be said that nitrous oxid here produces no irritation whatever.

Vomiting.—Nausea and vomiting are not more frequent than when no anesthetic is used. It has been stated that in labor vomiting is sometimes controlled by the administration of this gas. While I have not observed this, it would seem that, because it relieves pain and protects against exhaustion (shock), any effect that nitrous oxid might have in connection with vomiting would be inhibitory. Winckle reports (1890) a case of vomiting controlled with nitrous oxid.

Muscle Tone.—There is no loss of muscle tone such as occurs with chloroform and ether, the normal contractile power of all muscles, voluntary and involuntary, being unimpaired by nitrous oxid. Thus the mother is protected to a considerable degree against postpartum hemorrhage. The firm, postpartum contraction of the uterus, hastening its involution, renders less likely the entrance of infectious organisms through the uterine wall. Ergot is rarely necessary after a properly conducted nitrous oxid labor.

Bacterial Invasion.—Ether lowers the hemoglobin content of the blood to such a degree that it returns to normal only after a period of several days; it also reduces the number of antibodies, and interferes with the normal activity of the phagocytes, impairing thereby to a consideable extent, the normal resistance of the body against pathogenic bacteria. (Fenton B. Turck, of Chicago).

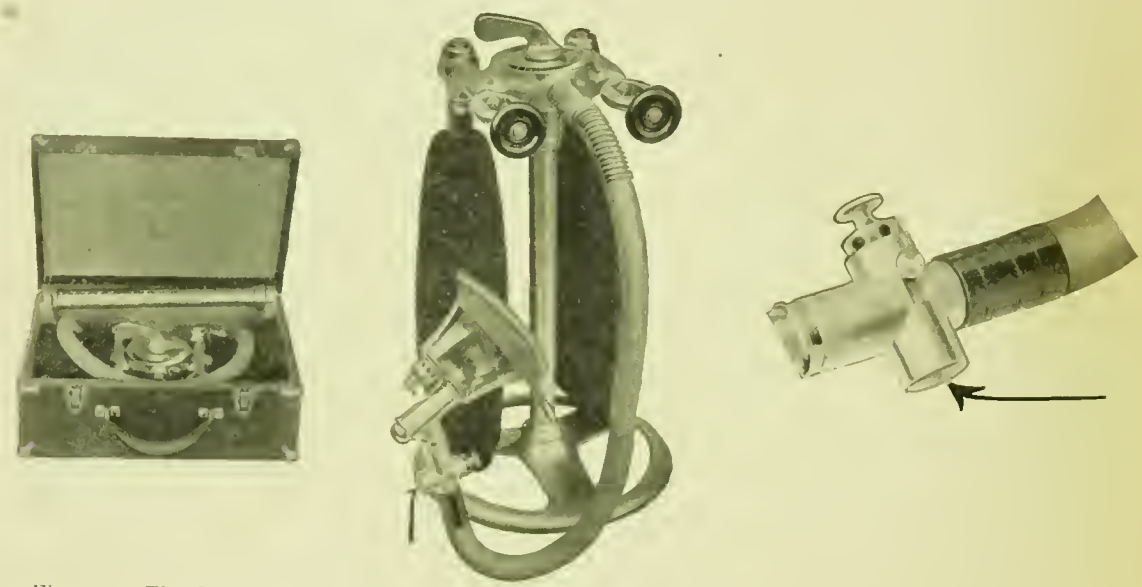


Figure 3. The Clark apparatus for use during labor. Assembled for use; packed for transportation and showing the trigger-attachment for self-control of gases during administration.

Graham, formerly of Chicago, now of Mason City, Iowa, establishes a close relationship between chloroform and the heretofore frequently reported hemorrhagic diseases of the newborn. Unlike these drugs, nitrous oxid produces but slight and transitory decrease of hemoglobin when administered to the degree necesary for major surgery, and no determinable decrease in resistance to bacterial infection. Neither is it credited with any post-anesthetic tissue changes that have yet been determined.

Exhaustion.—Under the proper administration of nitrous oxid in labor, the patient is not exhausted, mentally or physically. The general

postpartum condition is better than in cases delivered without an anesthetic, or with the anesthetic applied only during the last few minutes, as is the common custom with ether. The observer is impresed with the vigorous physical and mental postpartum condition of these patients. They display little or none of the usual depleted appearance of the woman having labored without analgesia.

A notable result of this protection against exhaustion of the mother and her freedom from blood and tissue changes, is manifest by the first week's progress of the babe. With the mother vigorous and physiologically normal, lactation is of early appearance and the breast milk of good quality, with the result that the babe is early and well fed. It does not exhibit the annoying symptoms of hunger, crying and

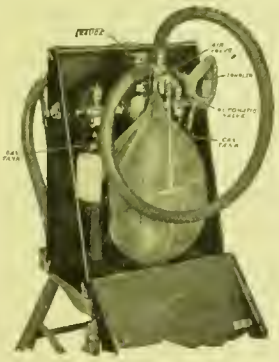


Figure 4. McKesson apparatus for administration of nitrous oxid, or nitrous oxid-oxygen during labor. The gases flow only during inspiration. Rebreathing can also be utilized during continuous analgesia or anesthesia.

restlessness, observed so frequently with the older methods of confinement. It need not wait 2 or 3 days for *the milk to come in.* Its progress is better in general. So manifest is this, that it is repeatedly remarked by nurses of experience in obstetrics. The proportionate loss of its initial body weight is apparently less, and its commencement to gain is earlier of occurrence.

The analgesia baby does not show intestinal distress to the same degree as the one born of an etherized or exhausted mother, and is apparently able to digest and assimilate its food to better advantage, from birth. This generally better state of affairs in the babe is dependent entirely upon the vigorous condition of the mother, and represents one of the most commendable attributes of nitrous oxid in labor.

Following delivery, some mothers are wide-awake and talkative others show a normal tendency to sleep. The early puerperium is pleasanter, the mother, requiring comparatively little attention. So constant is this that it also is noticed and appreciated by the nurse.

Convalescence.—There is an actual shortening of the convalescent period. More rapid involution, more favorable recuperation in general, renders it advisable to permit these patients to leave the bed a day or two earlier. They are actually a day or two nearer the norm

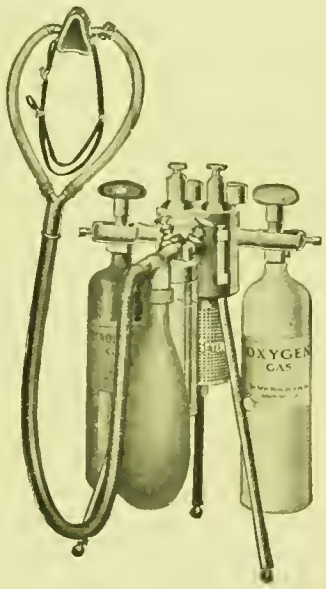


Figure 5. The Teter apparatus for the administration of nitrous oxid-oxygen for analgesia and anesthesia in obstetrics.

at the end of the first week, and confinement longer than necessary is harmful in any case. Fewer visits to the bedside are required, and the freedom from annoyance of little things wrong during this period is noticeable to the physician.

With nitrous oxid the patient secures physical relief from suffering to a greater extent than is usually secured with the obstetric administration of ether. There is not suffering, and forgetfulness of it; but freedom from suffering, with no unpleasant memories.

General Observations During Administration.—During administration the patient usually is quiet. Cases occur occasionally in

which this is reversed. The result should be regarded as unfavorable if the patient moves sufficiently to disarrange the linens or to interfere with proper aseptic technic. *It is inspiring to see a woman in labor, the foetal head widely distending the vaginal orifice, controlling all her volitional resources in response to suggestions of the operator, and withal, apparently free from pain.*

Variation in the Degree of Relief.—Some women claim but little relief with nitrous oxid analgesia. Some patients are disappointing in this respect and remain so throughout the labor. The greater number of women, however, who early in labor complain that there is no relief, quiet down and become favorable subjects after the first half hour's administration. These at the start frequently manifest a desire to go fast asleep with each pain. It is my practice with *self-administration* to permit this in many instances, knowing from experience that the patient will usually, after a few pains, appreciate that analgesia does provide sufficient relief, and will hold her own administration at the analgesic stage rather than experience the slight sensation of suffocation which often accompanies rapid nitrous oxid narcosis. In permitting narcosis early and allowing the patient to learn the difference between it and analgesia, an unfavorable patient is often converted into a satisfactory one.

Cases in which analgesia is not sufficient to control the suffering are few. There is some variation of relief as well as some interesting mental perversion. Postpartum discussion brings forth varying statements from mothers. A majority state that, while they appreciated all that was going on about them, felt the uterine contractions and were cognizant of delivery, they did not suffer. The pain was minimized or abolished. Occasionally one will say *"It hurt, but I did not mind it,"* and one good woman reported to me that she knew it was hurting, but it was her impression that *"it was hurting Mrs. McGinty who lived across the street, and it served her right."*

Women manifest pain in different ways. They may groan, squirm, mutter their suffering, and so forth, but these manifestations are often subconscious and are not remembered, satisfaction being expressed by the patient immediately the pain is past. This would seem to be amnesia, and perhaps in some cases amnesia has its part in this procedure.

However, a labor conducted under nitrous oxid analgesia, to be considered successful, must satisfy the patient.

Rapid Delivery.—In conducting his first few cases with this method the physician must be alert. The apparent suffering is often so small that he is liable to be misled as to the actual progress, and not recognize an imminent birth. My own daughter was born while the physician was scrubbing up for an examination, and I, grossly culpable, was standing idly by the bed.

Cummulative Effect of Analgesia.—It is interesting to note that all cases do better after the first half hour's application. There are two possible reasons for this. (1) The effect of nitrous oxid in small doses over a long period of time as a nerve sedative; and (2) the patient during this period, having gained confidence in the method, co-operates with more intelligence.

EFFECTS OF NITROUS OXID ON THE BABE

Nitrous oxid as administered today to the parturient woman, seems to have no ill effect on the babe, either directly or indirectly. Unlike other anesthetics, gas is not transmitted to the babe *in utero* in anesthetic doses. This is demonstrated by the early resusciation of infants born by Caesarian section under nitrous oxid anesthesia.

Nitrous Oxid Not Transmitted to the Babe.—During my early experience with this work (1910-1911), anxiety to totally abolish all pain, led to the frequent faulty administration of too much gas. Many times during a single labor, with individual pain administration, the mother would be rendered anoxhemic to the degree of deep cyanosis and vigorous muscular spasm, this occurring most frequently during the last hour of labor. It was noted that babies born of mothers who were at the moment of birth deeply cyanosed, were not blue. Their color was usually normal, comparing favorably with the color of newborn infants in cases conducted without anesthesia. There were no unfavorable manifestations in these babies, resuscitation being the same as in the well-conducted case. This was at first remarkable to us, but is now satisfactorily explained on the following basis:

Under individual pain administration the babe in utero or in the birth canal receives but little nitrous oxid from the mother, no matter how great may be the excess of gas in the mother's blood during the acme of contraction.

Administration of the gas is begun with the first evidence of each pain. Anesthesia progresses to the point of greatest depth usually at the acme of contraction, the first evidence of anoxhemia becoming mnnifest at this time, During the period of induction, when the gas is entering the blood of the mother, the uterus is contracting so that there is little, if any, interchange of foetal and maternal blood. The babe lives during the uterine contraction upon well oxygenated placental blood accumulated between pains. The anesthetic is removed at the acme of contraction, and considering that only 10 to 20 seconds are necessary for the removal of the excess nitrous oxid from the blood of the mother; also that during the relaxation period there is still little interchange of blood, it becomes evident that the blood of the fœtus receives but little nitrous oxid at any time. By the time the uterus is relaxed sufficiently to permit an interchange of blood through its walls, the blood of the mother is almost free of nitrous oxid and is again well oxygenated.

In continuous analgesia the necessary dose of nitrous oxid is so small that, were it given to the babe direct, it would hardly be sufficient to anesthetize.

Early Resuscitation.—Artificial resuscitation of the babe of normal labor under nitrous oxid is rare. Signs of life appear promptly in all cases, unless there is interference from another source. In the majority of cases the babe cries within 5 seconds after delivery, and not infrequently before the body is born.

Blue babies are no more frequent in nitrous oxid labor than in labor under any other circumstances.

TIME LIMIT OF ADMINISTRATION.

Time Limit of Administration.—In this there is no rule which holds so well as that which provides for the application of the gas when suffering is sufficient to warrant it. There is hardly a time limit to nitrous oxid analgesia. It has been given in some instances as long as 10 hours. I have given it several times for 6 to 8 hours. There is but slight, if any, manifest difference in the condition of the mother or babe, whether nitrous oxid analgesia has been administered for from 2 to 6 or more hours. The mother, having had the gas but 2 hours and having suffered considerably prior to its application, might present some evidence of exhaustion as compared to the other. It is better, as a rule, to begin early. Good results are more easily secured, and the patient is better protected against exhaustion.

Prolonged Administration.—It is interesting here to recall Winckle's statement that: *"Women to whom it is not administered until the stage of expulsion can seldom be induced to inhale it quietly, while when administered in the first stage of labor its beneficial action is at once felt and extends to the second stage."* This is notably true today, except that our more perfect equipment for handling the gas enables us to start late and provide considerable relief during expulsion. The time will soon come when this gas may be left with the nurse or experienced attendant, and the woman in labor be enabled, by self-administration, to secure relief safely with analgesia for any number of hours, leaving the physician free to come and go at will.

EFFECT OF NITROUS OXID ON THE PROGRESS OF LABOR

Ether or chloroform retards the progress of labor by inhibiting contraction of the uterine and skeletal muscles. Morphin retards by a general depression of the entire nervous sensorium. Nitrous oxid, to the stage of analgesia, affords control of the progress of labor in a way that cannot be secured with any other agent. There has been considerable discussion regarding the apparent shortening of labor under nitrous oxid. That the second stage is shortened in the majority of cases, there can be no doubt.

It has been supposed that nitrous oxid stimulates uterine contraction. However, it probably has no immediate effect on this muscle. Given to the stage of analgesia, this gas after the first half-hour produces a relaxation of all muscles to a degree similar to that of normal sleep.

Volitional Assistance by the Patient.—The mother, laboring with no relief from pain, will

usually make but little voluntary effort to assist the progress of labor. To bear down increases her suffering. Under gas analgesia, her freedom from pain enables her to render voluntary assistance to good effect in hastening birth. McKesson, of Toledo, has observed that the progress of labor with continuous nitrous oxid narcosis is influenced but little if at all, there being no voluntary assistance on the part of the mother.

GENERAL DISCUSSION OF ANALGESIA

Analgesia, as our dictionaries define it, is the loss of the sense of pain perception without loss of the sense of touch or general consciousness. It occurs during the induction of narcosis with any anesthetic agent, and consists of a depression of the centers of pain perception, usually in depth proportionate to the dose administered.

Nitrous oxid, because of its reliability of action and ease with which its dosage can be regulated, becomes our most satisfactory agent for the induction of useful analgesia. Properly administered, this gas produces an operative state of progressively increasing depth until it is terminated in narcosis.

The so-called *painful stage* which has been said to occur at a point just beyond analgesia with nitrous oxid, does not occur with sufficient regularity to constitute a definite state. It represents a form of mild excitement and should be considered accidental. Attempted surgical procedure during this state will fail to be considered painless by the patient.

Under the progressive administration of nitrous oxid the pain sense is totally abolished in all cases before consciousness is lost, but so shortly before that these two phenomena almost meet, and it is difficult at times to maintain analgesia within the narrow latitude separating them. This state represents total analgesia, with pain perception entirely abolished, and the patient still in possession of her mental faculties, although these are considerably depressed. In this state the patient will respond but slowly and with apparent effort, to suggestion; and to become effective here, suggestion must often be made and repeated with the forcefulness of command.

Total Analgesia Not Necessary.—It is not necessary in all cases to secure the total abolition of pain perception. The pain of different operations varies in degree, and it is necessary only that we induce analgesia to a depth sufficient to abolish perception of the particular pain being dealt with.

Analgesia is peculiarly fitted to the woman in labor. Here there is no fear as of an operation, and this freedom from fear renders nitrous oxid analgesia more applicable. Labor pains as a rule are controlled with comparatively light analgesia, the deeper state being required only during the latter part of the second stage and at delivery.

The depth of analgesia is dependent upon the amount of nitrous oxid absorbed by the nerve cell, and this may be regulated at any point by adjusting the gas mixture.

Analgesia becomes deeper to a slight extent as it is continued over a period of time with a set mixture. For example, supposing that the mixture in a given case be nitrous oxid 65 and air 35 (or nitrous oxid 82 and oxygen 18) with resulting continuous total analgesia; this patient after the first 5 to 15 minutes will usually lapse quietly into narcosis.

Suggestion.—The patient under analgesia is more susceptible to suggestion and more obedient to instructions than otherwise. With the depression of pain perception by nitrous oxid there is a concomitant depression of the entire central nervous system. As with any other anesthetic agent, the nerve centers for various functions are not all affected at the same time nor to the same extent, but if the gas in narcotic dosage be continued, the centers one following another are progressively depressed, and finally paralyzed. Among the earliest of these functions to succumb is volition, thereby rendering its possessor more susceptible to the influence of the will of others. Sometimes this depression of the will is so marked that the patient obeys as if hypnotized.

TYPES OF PATIENTS FROM THE STANDPOINT OF RESULTS TO BE EXPECTED

This discussion deals with the usual types as they occur in practice and their reaction in general to nitrous oxid analgesia in confinement.

No rule holds in all cases. We cannot always forecast the result in any individual. Good results may obtain in patients from

whom but little was expected; and the anticipated favorable case may prove a failure. However, in a general way a classification of types can be made and the result anticipated with some degree of reliability. For the purpose of presentation it is well to consider two general classes; namely, *physical* and *mental*.

MENTAL TYPES.—As determined by the earlier investigators (1880-1886), suffering is usually relieved in proportion to the intelligence of the patients. The amount of education and training the patient has had is not so important as ordinary, natural intelligence and the desire to do her part. The patient of sluggish mentality may fail to appreciate her part of the technic and because of this a good result is more difficult of accomplishment.

Nervous Patients.—The extremely nervous type, whether high or low mentality, is apt to give trouble at the start, and occasionally will become so hysterical as to be uncontrollable with analgesia. This type is fearful and being unable to appreciate analgesia, accepts every sensation associated with her labor, as pain.

Mutiparae.—Multiparae are usually better patients. Having suffered in previous labors, they are able to appreciate the relief of analgesia, and it is this class that seem most grateful to the physician for the service he has rendered. However, there is a small class of multiparae, mentally and physically lazy, who do not care particularly how their babe is delivered so long as they are not disturbed. This type may not do well under any form of nitrous oxid application other than continuous anesthesia. Here the novelty of confinement, which serves to held the primipara of the same type, is gone.

Primiparae.—Primiparae are frequently disappointing, although satisfactory results are as easily secured in these as in multiparae who are experiencing their first labor under this method. The disappointment rests upon the fact that they are unable to appreciate the suffering which they have been spared. Some of my best results have occurred in primiparae, who later complained that labor was a terrible circumstance. Not knowing what to expect in this new experience, they are frightened, and more tact is required in handling them.

The second delivery under gas in the same mother is obviously more easily handled than the first. She has learned her part of the technic and is able to assist to greater advantage.

PHYSICAL TYPES.—Mental conditions being equal, better results are usually obtained in the small woman. The respiratory capacity influences to some extent, the rapidity of induction. The patient with small respiratory area may have trouble in securing analgesia quickly enough to meet and control the fulminant pain.

Alcoholics and drug habitues respond more favorably to analgesia than to narcosis.

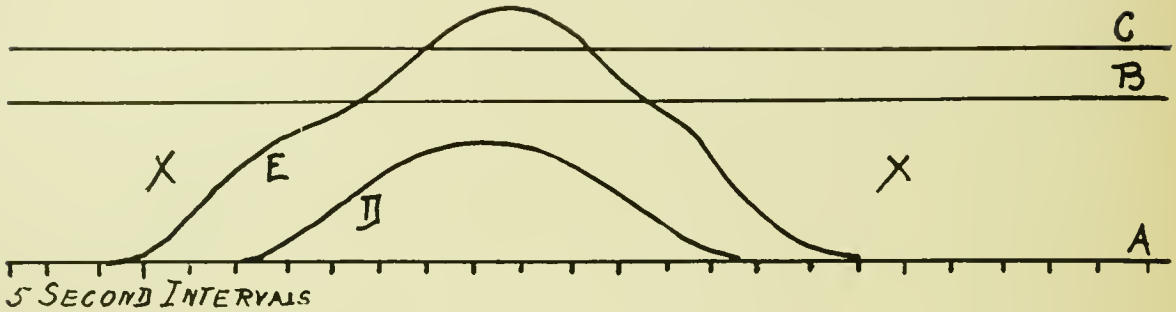
Alcoholics and drug habituese respond more favorably in analgesia than would be expected, judging from our knowledge of their usual resistance to surgical anesthesia.

NARCOTICS IN CONNECTION WITH NITROUS OXID IN OBSTETRICS

There is considerable variation of opinion among those who are now employing nitrous oxid in labor as to the value and place of the narcotic in connection with this work. Some operators employ narcotics throughout labor, practically according to the Freiburg method, using nitrous oxid analgesia to support the action of the narcotics, as labor nears completion. This might be of value in certain difficult cases, but as a routine method it is not productive of such satisfactory results as nitrous oxid alone.

Indications.—Narcotics properly administered in the early first stage are so frequently of value that it has become almost a routine practice in my work. The early administration of the narcotic serves to relieve the small suffering of the first stage and bring the patient to the second stage in better condition both mentally and physically for work.

Respiratory Depression.—The danger of the morphin group administered to the mother in labor, falls upon the babe. It is greater or less, depending upon the time of its administration. If given early enough that it is eliminated before the babe is born, it is safe; but when given later than 4 to 6 hours before delivery the babe is apt to arrive with its respiratory center so depressed that it is resuscitated with difficulty or is not resuscitated. The only cases under nitrous oxid analgesia in which there is difficulty of resuscitation are those in which morphin has been administered late. Nitrous oxid in these cases has no influence



Key Chart. A, normal sensation; B, total analgesia; C, beginning narcosis; D, pain curve; E, analgesia curve; F, intervals of time; XX, latitude of relative a nalgesia.

over the effect of morphin upon the babe, except to a slight degree where extensive rebreathing has been employed during the last part of labor, in which case the accumulated carbon dioxid in the foetal blood may assist slightly toward the stimulation of respiration.

Except in rare instances where the pains are severe and fulminant in type, intermittent gas analgesia alone, is more successful than when combined with morphin. The depression of the sensory centers produced by morphin renders the beginning of contractions unappreciated by the patient, and because of this the gas is apt to be started too late to control the pain, unless, as suggested by Lynch, the operator determines for himself the commencement of each contraction, by palpation, not depending upon the signal from the patient to start the gas, (Chart I.)

Results are usually better with the mentality of the patient not depressed. The hypodermatic narcotics may sometimes quiet the nervous patient and render nitrous oxid analgesia more favorable.

Narcotics have been frequently used to good effect in connection with gas analgesia to lessen the violence and frequency of contractions of the irritable uterus. To control excessive uterine contraction late in labor other methods are preferable.

ANALGESIA AND PERINEAL LACERATION

Without Analgesia.—There is no question as to the relative frequency of perineal injury without anesthetic, and with nitrous oxid properly applied. The number and degree of perineal tears is considerably diminished in the latter case. With no anesthetic the mother, usually in a state of nervous exhaustion from labor up to this point, is rendered more or less uncontrollable by the pain of the stretching perineum. Whereas, having been able to lessen her suffring to some extent during the earlier part of the second stage by withholding voluntary assistance, at this point with the head distending the vaginal orifice, the reflex stimulation of pain renders voluntary relaxation almost impossible. Her tendency is to throw into forceful activity all of her expulsive power. Advancement of the head instead of being retarded is more rapid than at any other

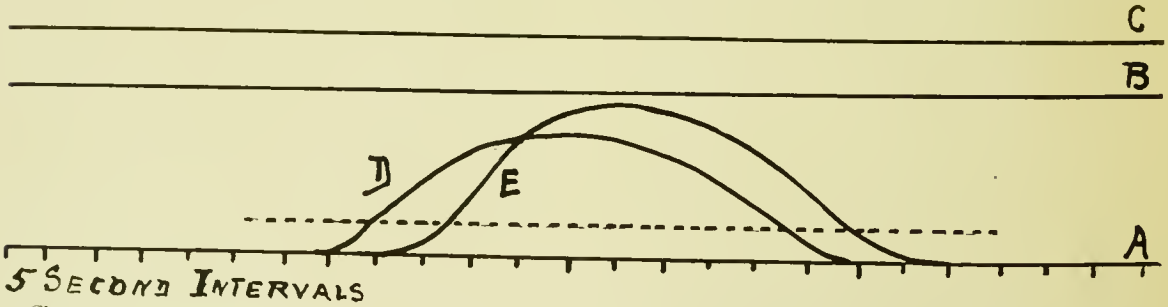


Chart I. Diagramatic illustration of the manner in which morphin depression of pain perception interferes with the timely application of gas, in intermittent analgesia. The dotted line represents the morphin elevation of the threshold of pain stimulus. Pain below this line is not perceived.

time. The operator has little control over this patient, and as a rule she presents a condition decidedly unfavorable for delivery.

With Analgesia.—Under nitrous oxid analgesia a different picture presents. Being free from pain and not exhausted, the patient is quiet and able to co-operate. The perineum is not rigid; it is considerably relaxed as compared with the former case, and the mother is able to relax the voluntary muscles of expulsion at the command of the operator. In general, she presents a satisfactory state for proper delivery. The advancement of the head, which earlier in the second stage was properly hastened by her voluntary expulsive efforts, is here retarded by her ability to relax. The physician is able to manipulate the perineum and hold back the head at will, permitting the vaginal orifice to dilate slowly. The only possible improvement over this presentation with regard to protection against perineal laceration, would be the addition of a total relaxation of the perineal muscles.

Refractive Patients.—Such is a description of the favorabe result. Occasionally, however, the patient during delivery does not present such an ideal condition. When continuous deep analgesia does not entirely abolish the pain at this period, the patient will not be so quiet nor so easily controlled. There may be some movement with a tendency to voluntary expulsion, and the physician finds it necessary to command, insistently, in order to maintain control. A patient who is not quieted during this period by analgesia, is better delivered under light narcosis. Analgesia provides better control than narcosis only when it is sufficient to relieve the suffering. It is my practice to permit continuous analgesia in all cases during this period and in most cases during the preceding period of rapid pains. Better delivery is to be expected in those cases in which continuous analgesia has been maintained for half an hour or so before delivery. To begin the application of nitrous oxid during the delivery period will not secure the same satisfactory result.

Etherization.—Ether contributes a greater relaxation of the perineal muscles than nitrous oxid, and a slower advancement is obtained under proper administration. It is the practice of some operators to change from nitrous oxid analgesia to ether for delivery, but when this change is made late there is apt to result an unquiet and less satisfactory state. The patient is usually quieter for delivery under a continuation of deep analgesia than with a late change to ether, and it is doubtful whether, under these circumstances, ether diminishes the number and severity of lacerations. Where laceration seems inevitable, epesiotomy is performed under analgesia.

Anesthesia for Delivery.—If a momentary state of anesthesia is anticipated for delivery, the reaction of the patient in this respect should be determined earlier, as occasionally a patient in passing from analgesia to narcosis is rendered unquiet, and an unquiet patient at this important moment is not desirable.

It is probable that at the present time perineal laceration is less frequent with ether than with nitrous oxid. However, as the technic of nitrous oxid is better understood by both patient and physician, this is likely to be reversed.

Internal Lacerations.—While it is often possible to prevent the external tear, analgesia seems to afford no protection against injury to the vaginal wall, and it is always well to examine carefully for internal lacerations. It is not improbable that the more rapid advance of the head through the vaginal canal, together with the absence of pain as a guide, renders the internal laceration of more frequent occurrence with analgesia than otherwise. I have found the vaginal wall torn severely, in cases delivered without the slightest abrasion externally.

PERINEAL INFILTRATION

Little of this has been done to date. It has been practiced by some and abandoned, while others report increasingly good results. Undoubtedly in certain cases, proper perineal infiltration combined with nitrous oxid analgesia offers worthy advantages.

Carl L. Hoag, of San Francisco, in the study of a series of 50 cases, reports striking results with this combination.

As the head begins to distend the perineum, the vulval edges are turned back and the levator ani, and the perineal body thoroughly infiltrated, introducing the needle through the vaginal mucous membrane, to lessen the likelihood of infection. A generous quantity of a

1-4 per cent. solution of novocain is injected.

The effect reported is a total relaxation of the perineum and an absolutely painless delivery, general analgesia being necessary only in sufficient depth to control the pain of the uterine contractions. The patient remains quieter and is under better control than with nitrous oxid alone. This method is credited with fewer perineal injuries than any other method of delivery. In cases where the advancement is slow it may be necessary to reinfiltrate before delivery is completed, the effect of novocain lasting only from 30 to 40 minutes. This inconvenience may be avoided by following the novocain immediately with a solution of quinin urea hydrochlorid.

It is advisable to infiltrate before there is any distension. It is easier to prevent the muscle spasm than to relieve it, and the muscle in spasm is more difficult of infiltration. In 50 cases with this method, Hoag has observed nothing deeper than a first degree tear, and claims but few of these.

Novocain seems to exert no effect on the babe; at least none has been noted, the babe having little opportunity to absorb any of the drug.

Those who have employed perineal infiltration in this connection and have abandoned it, claim no disadvantages and no unfavorable circumstances attendant upon its application. The reasons given for its discontinuance are usually that the advantages gained by its use are not sufficient to warrant the inconvenience of its employment in all cases.

I am impressed that this adjunct to nitrous oxid analgesia will find a valuable place in certain cases, with disproportionately small vaginal outlets. Hoag properly urges further study of the method.

NITROUS OXID AND OBSTETRIC OPERATIONS

Low Forceps.—The application of nitrous oxid in major obstetric surgery is to be governed by the same anesthetic rules that apply in all major surgery. The more common, smaller operations which we frequently encounter can be accomplished under nitrous oxid analgesia with little or no difficulty. Usually a low forceps delivery is more easily accomplished under proper analgesia than under narcosis, because of the fact that the patient can assist the operator. It is to be remembered, however, that the proper administration of nitrous oxid during labor renders instrumental delivery less frequently necessary. I have yet to witness the first uterine exhaustion where analgesia was started with or before full dilitation.

Version.—Version under nitrous oxid analgesia is at present of doubtful accomplishment. Successful version is claimed by a few operators, but it would seem that, because of the value of muscular relaxation in this operation, ether is better.

Incomplete Abortion.—Analgesia has proven satisfactory for emptying the uterus following incomplete abortion. In early abortion the cervix can be thoroughly dilated and the uterus cleansed with curette or finger. Results in this work are surprisingly satisfactory in the majority of cases. I am, however, no longer disappointed when an occasional patient fails to respond properly.

Perineal Repair.—It is my rule to make all immediate repairs under the same state of analgesia as that used for delivery and this is accomplished usually without trouble.

It is necessary to explain more definitely to the patient the nature of analgesia, because her mental attitude toward the operation is not so favorable as toward labor. Labor is a physiological function; perineal repair is an operation in which instruments are employed.

It is noteworthy that not infrequently a patient who has satisfactorily completed delivery under analgesia, flinches under the same state during perineal repair. She will usually object to the first sutures more than to the last, and objects not so much to the penetration of the tissues by the needle as to the tugging of the sutures when they are tied. It is better to place all sutures before beginning to tie.

Because of the lapse of time between delivery and readiness to operate, it is advisable to allow 2 or 3 minutes of analgesia before beginning. Analgesia, as stated, is more satisfactory after the first few minutes of administration. Although thoroughness is never neglected, the operator will learn after a few trials that it is to his advantage to handle the tissues as gently as possible.

For this work deepest analgesia is employed.

Self-administration with the nasal inhaler is here particularly applicable.

Novocain Infiltration.—Cases in which infiltration of the perineum has been practiced for delivery, are repaired under the resultant local anesthesia alone. Here, however, repair must be made early unless the novacain anesthesia has been supported with quinin urea hydrochlorid.

Primary repair of the cervix under analgesia is yet an unsettled question. Anesthesia is usually preferred for this work.

POSSIBLE ACCIDENTS WITH NITROUS OXID

In the practice of obstetrics we must accept cases as they come—the bad risks as well as the good. We will be called to deliver a woman in whom there exists a cardiovascular degeneration. It is not possible in every case to determine the presence of such conditions beforehand, hence in discussing the question of possible accident here, we must consider the abnormal as well as the normal patient.

Death under nitrous oxid may occur as a result of three conditions: (1) asphyxia, (2) cardiac dilatation, and (3) apoplexy. In the individual of normal cardiovascular system, asphyxia can be the only cause, and death due to accidental asphyxia from nitrous oxid can occur only as the result of the greatest carelessness.

Normal Patients.—With the administration of pure nitrous oxid, cyanosis and muscular jactitation appear, usually about the time of narcosis. The anoxhemic muscular spasm (jactitation) makes it first appearance in the extremities—farthest from the center of circulation, and progresses thence to the body and neck, closure of the glottis occurring after the spasm has existed for some seconds.

It was the custom until a few years ago, in the general application of laughing gas for tooth extraction, to carry the patient frequently to the point of clonic spasm of the glottis (beginning asphyxia), and even with this crude technic, statistics present an exceedingly low mortality. There is ample time to remove the inhaler between the inauguration of the spasm and its extension to the glottis. With the anesthetic stopped at any time during this period, the normal patient will not be harmed. In fact, nitrous oxid anesthesia has been carried beyond this period innumerable times without accident.

Cardiovascular Degeneration.—Accident to the patient with cardiovascular degeneration is less likely during labor under nitrous oxid analgesia than with any other conduct of the case. With such conditions present the important indication is an easy labor with as little suffering as possible. Blood pressure is elevated but little (6 to 12 millimetres) during the proper induction and maintenance of nitrous oxid anesthesia. It begins to mount rapidly with the occurrence of cyanosis or other manifestations of anoxhemia, and with forced continuation of the gas, it rises as much as 100 millimetres in some cases before the glottis is closed. This rapid elevation in the presence of atheroma or degenerative myocarditis, renders apoplexy or acute cardiac dilatation not unlikely. It was my fortune—or misfortune—to witness such cardiac dilatation following a nitrous oxid narcosis for tooth extraction. The point of interest in this case was that the patient did not collapse until she had been raised from the horizontal to the upright position, about five minutes after recovery from the narcosis.

Although death or serious accident with nitrous oxid in obstetrics, is quite improbable, it nevertheless behooves us to exercise at least, ordinary care in applying this method.

Safety lies in the avoidance of asphyxial manifestations.

COST OF ADMINISTRATION

The cost of administration of nitrous oxid in obstetrics is worthy of a brief discussion here. It cannot be compared with the higher cost of nitrous oxid-oxygen anesthesia for major surgery.

The amount of gas consumed by different patients varies considerably and only a rough estimate of the cost in a general way is possible. I have maintained intermittent analgesia for as long as 6 hours in the same case without emptying one 100-gallon cylinder of gas, while in another case recalled, the patient consumed, under the same method, 100 gallons of the gas in a few minutes less than one hour. Usually this small cylinder can be expected to carry the patient through the last 2 or 3 hours of labor. It has been my observa-

tion that little if any more gas is consumed with continuous analgesia, during the last hour of labor, than with intermittent induction.

As a rule the beginner with this method uses more gas than is necessary.

My plan is to carry to every case, 2 cylinders, one of which may be depleted. In only 4 cases have I found it necessary to send for additional gas.

GENERAL DISCUSSION OF TECHNIC.

There are many variations in the technic of nitrous oxid in obstetrics. They are all, however, based upon one fundamental principle; namely, the necessity of providing sufficient nitrous oxid to control the pain, together with enough oxygen to maintain adequate tissue respiration. Different as the technic of various men may seem, the results attained are practically the same. The following gas mixtures are advocated for routine application:

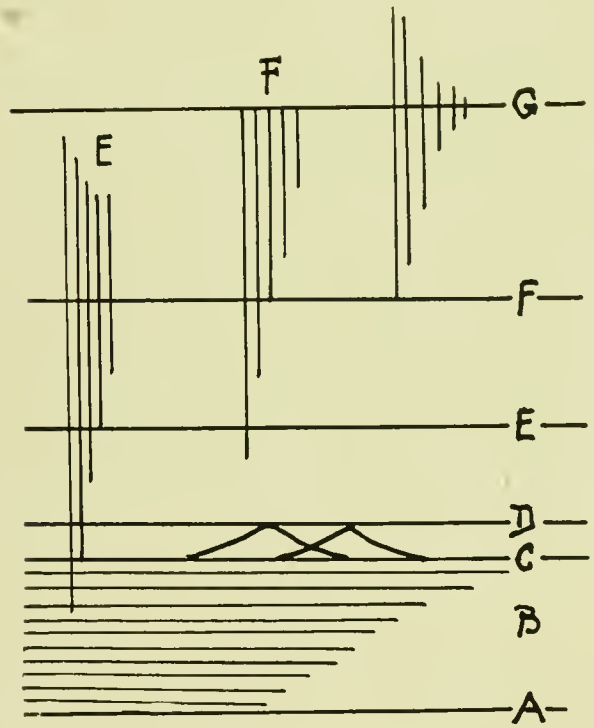


Chart 2. A, normal consciousness; B, relative analgesia; C, total analgesia; D, beginning narcosis; E, Cyanosis and jactitation; F, asphyxia, and closure of glottis; G, death. Schematic illustration of progressive phenomena occurring during the administration of nitrous oxid. The horizontal lines indicate the usual periods at which the phenomena occur. The vertical lines indicate individual reactions.

(1) Pure gas, or gas with 10 to 15 per cent. air, the dose being regulated by the number of inspirations, 6 to 10 for each pain.

(2) Pure gas for the first 2 or 3 inspirations, diluting the fourth and fifth with 2 per cent. oxygen, the subsequent inspirations receiving a higher oxygen dilution—20 to 30 per cent.

(3) The employment of set mixtures; that is, not changing during any single pain application.

(a) Nitrous oxid 80 per cent., oxygen 5 per cent., and the balance air.

(b) Nitrous oxid with 2 or 3 per cent. oxygen.

(c) Nitrous oxid with 5 to 15 per cent. air.

(d) (Some operators do not reckon dosage in gas percentages, but by the rate of gas delivery per hour). Nitrous oxid 30 to 80 gallons per hour, and oxygen 10 to 30 gallons, with the balance air.

Although at first thought these mixtures seem extremely variable, when they are considered in connection with the fundamental basis governing analgesia and narcosis, the variation it not great. Results with these mixtures may differ to a slight extent as to the quietude and rapidity of induction.

ANALGESIA—INDIVIDUAL PAIN ADMINISTRATION

The object here is to secure analgesia ahead of the pain, to maintain it to a depth corresponding to the severity of the pain throughout the entire uterine contraction, and to leave the patient free from gas in the intervals. (Chart 3).

The rapidity of induction of the analgetic state is influenced slightly in several ways:

Rate of Induction.—The greater respiratory capacity, by furnishing a broader alveolar absorption area will carry more gas into the blood, hence, other things being equal, it will shorten the induction period.

Assuming that pure gas (100 per cent.) is employed, rapidity of induction will vary in the same individual according to the residual air content of the lungs. The residual air in

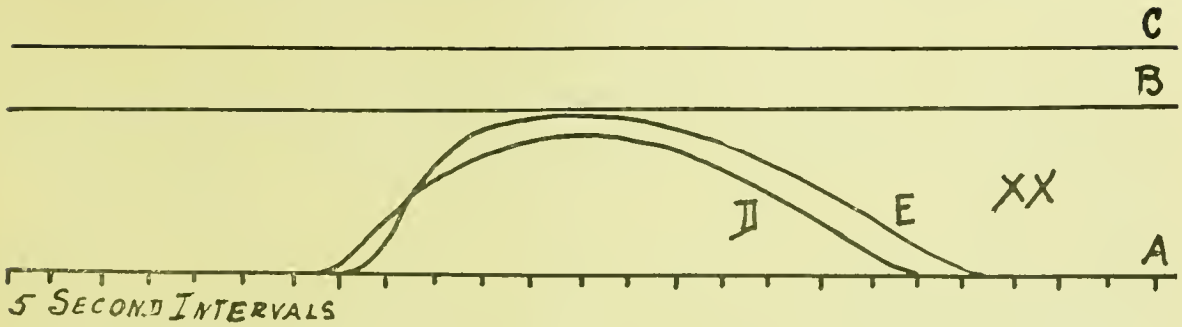


Chart 3. Illustrating the manner in which the pain is covered by analgesia in the usual case. A, base line; normal sensation; B, total analgesia; C, beginning narcosis; D, pain curve; E, analgesia curve; XX, Latitude of relative analgesia.

the lungs is sufficient to dilute the first inspiration of gas about one-half. With each subsequent inspiration the dilution become progressively and rapidly less, until all air in the lungs is displaced, after which undiluted gas is taken into the blood. There has been no accurate determination as to the number of respirations required to bring this about, and any estimate must be based only upon clinical observation. Probably this total displacement of air occurs between the third and sixth respiration. Where rebreathing is practiced from the beginning, total displacement is delayed perhaps one or two respirations longer, due to the apparent fact that a part of the air expired during the first few respirations is returned to the supply bag, to dilute the gas awaiting inspiration.

This observation presents a practical point. Where an extremely rapid induction is desired this may be better accomplished by starting the gas after forced expiration. Results of experiments conducted with reference to this are confirmatory.

The following observations were made in the same individual:

Self-administration; pure gas with face inhaler; no rebreathing. Beginning after forced expiration, narcosis—indicated by the removal of the inhaler—occurred with the tenth respiration. Beginning after ordinary expiration, narcosis occurred with the twelfth respiration. Beginning after normal inspiration, narcosis did not occur until the fourteenth respiration.

As with any other drug, patients manifest varying susceptibility to nitrous oxid. Assuming that this variation lies within the nerve cell, it becomes evident that although rapidity of induction depends in a measure upon the rapidity with which the gas is carried to the cell, it depends also upon the susceptibility of the nerve cell to its action. In studying the induction of nitrous oxid narcosis, we find the question of hemic anoxhemia, together with that of nerve cell susceptibility, governing almost entirely the quality and rapidity of induction.

The refractive individual, in whom the nerve cell depression by nitrous oxid is slow, will, with pure gas, manifest anoxhemia (cyanosis,

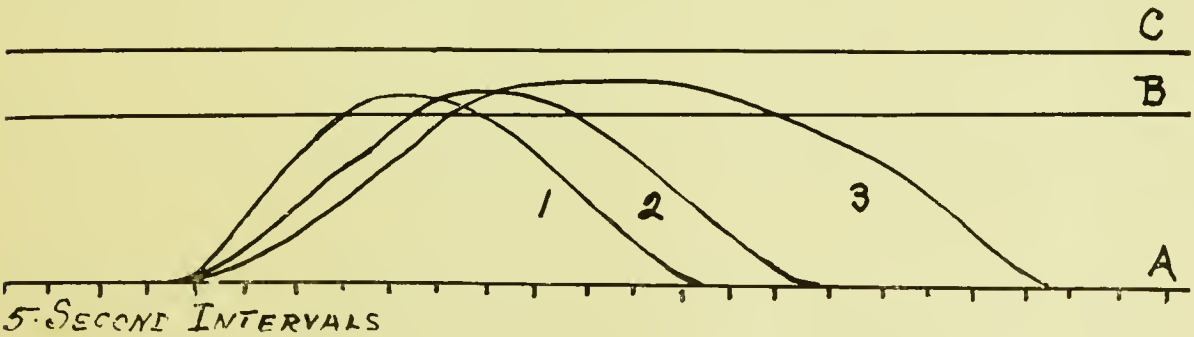


Chart 4. Comparative illustration of different types of analgesia obtained by a single application, withdrawing the inhaler at total analgesia. 1, Pure nitrous oxid (100 per cent.); 2, Nitrous oxid with 2 per cent. oxygen or 6 per cent. air; 3, Nitrous oxid with approximately 5 pere cent. oxygen or 15 per cent air.

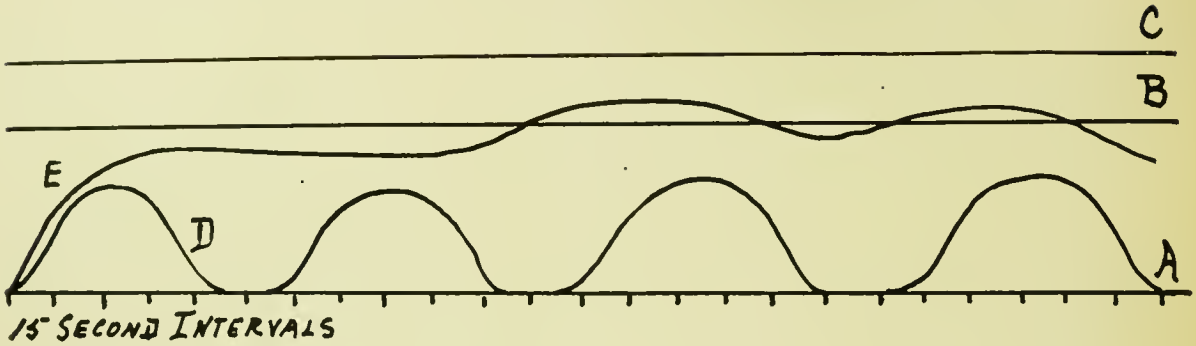


Chart 5. Illustrating the manner in which continuous analgesia covers the pains. A, normal sensation; B, total analgesia; C, beginning narcosis; D, pain curve; E, analgesia curve.

jactitation, and excitement) before the occurrence of narcosis. On the other hand, in the patient whose nerve cells rapidly succumb to the gas—the usual type—pure gas will produce narcosis before there are any manifestations of oxygen deprivation. It is rare to find in obstetric practice a patient so refractive that this gas cannot be successfully administered.

If adequate analgesia cannot be secured rapidly enough to abolish the pain, the *intermittent application* should be abandoned for *continuous analgesia*. The refractive individual can sometimes be handled successfully with intermittent administration, where the pains are of the slower type, by employing a lighter mixture, more oxygen or air and less gas.

Available Analgesia.—Analgesia or narcosis induced with undiluted nitrous oxid is not so long sustained after the removal of the mask, and is therefore not so satisfactory for the longer contractions. The state, however, can be prolonged by reapplying the inhaler after permitting one or two breaths of air. (Chart 4).

Usually the patient can be depended upon to indicate the approach of a pain.

In the usual case I have found that gas to a dosage of 85 per cent. with air, or 98 per cent. with oxygen, is productive of a quieter, longer and more satisfactory analgesia with induction of ample rapidity.

The recognition of the degree of analgesia necessary in this work depends entirely upon the suffering manifested by the patient.

Marked respiratory acceleration, change of color or jactitation, are evidences of a beginning anoxhemia and should be met with an immediate dilution of the gas mixture. This can be accomplished as a rule most conveniently by lifting the edge of the inhaler.

CONTINUOUS ANALGESIA

This is frequently necessary in order to secure satisfactory results. Toward the end of labor, or in any case in which the contractions are so rapid and severe as to render the individual pain administration difficult, continuous analgesia is indicated. (Chart 5). In these

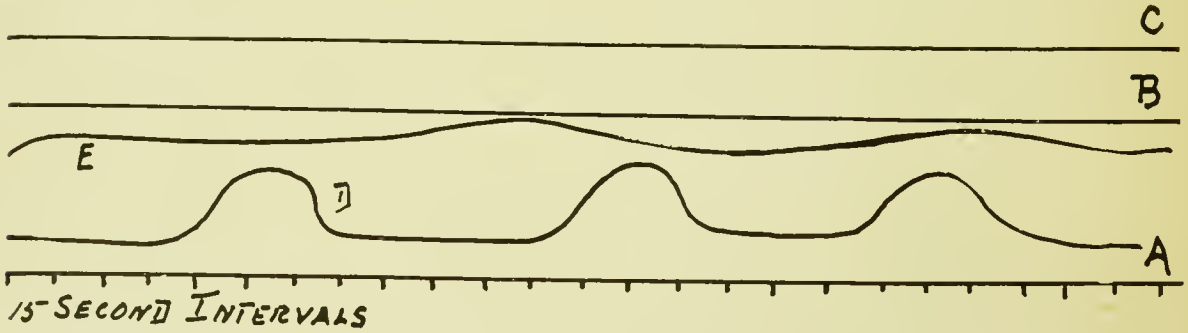


Chart 6. Illustrating the advantage of continuous analgesia in case of interval pain, due as a rule to pressure upon neighboring nerves.

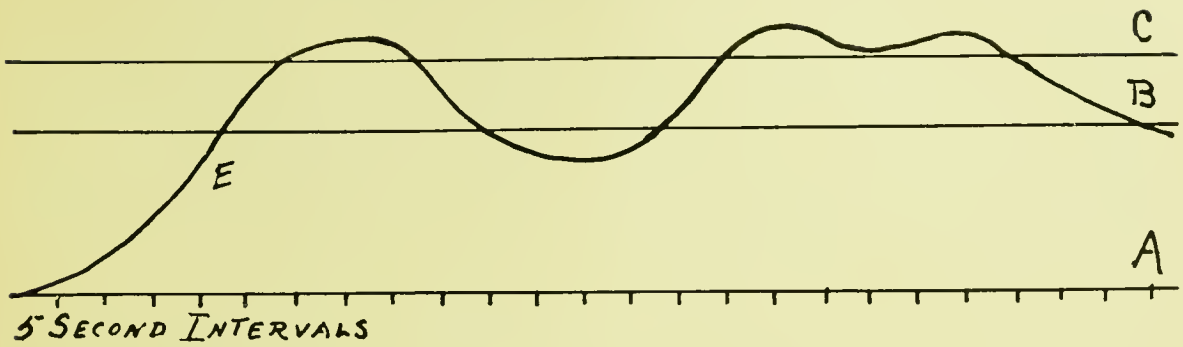


Chart 7. Continuous analgesia curve with self-administration; illustrating lapses into unconsciousness.

cases it affords greater relief to the mother and renders her more easily controlled. The gas mixture here depends upon the depth of analgesia indicated. Nitrous oxid with 30 to 70 per cent. air, or 15 to 30 per cent. oxygen, is the usual mixture employed. (Chart 6).

With selfadministration it is frequently advisable to employ a richer mixture (gas with 20 to 30 per cent. air) the patient governing the depth of her own analgesia by breathing through the mouth occasionally, prompted by the recognized sense of approaching narcosis. Unscientific as this may seem, the result is more satisfactory as a rule than with an attendant holding the inhaler. (Chart 7).

Not infrequently a patient who complains that analgesia is insufficient to relieve her suffering may be permitted to lapse into momentary narcosis and back into analgesia, with resulting greater relief, although the analgesia following the narcosis should be no deeper, judging from the standard of dosage, than that before. While this has been a frequent clinical observation, it is difficult to explain. (Chart 8).

It is possibly due to nerve cell retention of a part of the narcotic dose of nitrous oxid, for some time after the dose has been reduced; or it may depend upon a lingering psychic effect of the narcosis. From its constancy of occurrence, the former explanation would seem more likely.

The technic of permitting this lapse into narcosis is to increase the dose of gas by reducing the diluent. In returning to analgesia, the mixture is readjusted correspondent to that formerly employed.

INTERMITTENT NARCOSIS

This discussion refers to complete narcosis for each pain with complete recovery during intervals.

This is the least satisfactory method of administering nitrous oxid in labor—from the standpoint of both the physician and the patient. It is rare to find a case in which other methods herein described cannot be applied to better advantage.

To apply nitrous oxid at the beginning of a contraction and secure narcosis before the fastigium of the pain is reached, is to administer

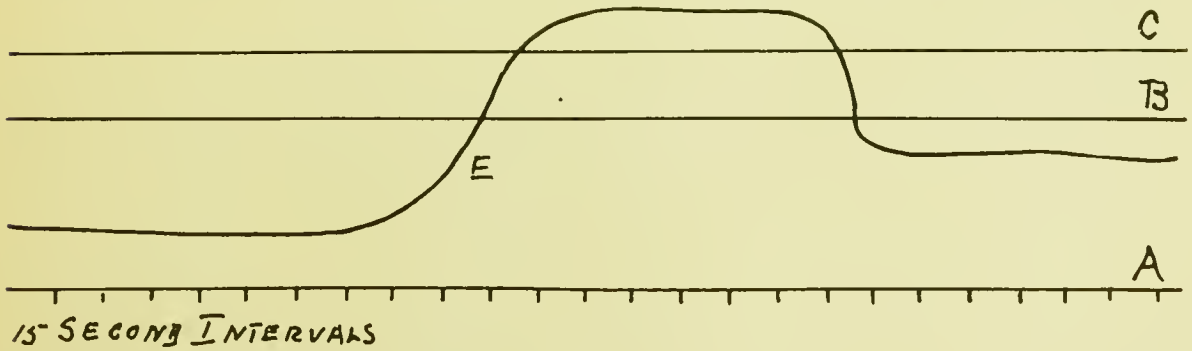


Chart 8. Continuous analgesia curve, showing apparent increased depth with the same gas mixture, after allowing a few moments of narcosis.

the gas too rapidly and in such high mixture that there frequently occurs anoxhemic manifestations, often with considerable concomiatnt excitement. With the self-administration intermittent narcosis is safe, the inhaler being always removed by the patient either by muscular relaxation or by the first intercurrent anoxhemia spasm. Although this method is safe, it is not satisfactory in most cases, particularly if it is repeated for each pain over a long period of time.

With an attendant holding the inhaler the possibility of accident is considerable. The only alarming manifestation that I have seen with nitrous oxid in labor, occurred with this method.

CASE REPORT: The patient had been anesthetized completely for each pain during a period of 1 1-2 hours. Gas and oxygen was the combination in use, but the necessity for rapid narcosis precluded the use of oxygen and there was slight cyanosis and jactitation with each induction. So far as relief from suffering was concerned, the case was satisfactory and the mother did not express any sense of discomfort, recovering each time quickly and remaining conscious throughout the intervals. During the recession period of one pain, and after the anesthetic had been entirely removed, the patient suddenly collapsed. Respiration ceased, eyes were staring with pupils widely dilated; color, which was not bad when the mask was removed, changed to blue and then to that flat, bluish-gray that none of us care to see the second time, even in the other fellow's patient. There was no rigidity; instead, the total relaxation of collapse. The anesthetist pressed forcibly on the anterior chest wall 2 or 3 times, after having pulled the tongue forward, and the patient began to come around. With 3 or 4 voluntary respirations she was again apparently normal.

The whole circumstance, from the application of the anesthetic, through narcosis, collapse and on to apparently normal recovery, occurred in approximately one minute. Examination of the heart after recovery disclosed nothing wrong. The pulse, according to the anesthetist, was increased but little above its previous rate, remaining about 100.

I am not prepared to state what happened in this case. I am convinced, however, that this occurrence was closely connected with that particular plan of administration, and such an occurrence is wholly undesirable.

With the patient holding the inhaler it is my plan to permit narcosis for the expression of the placenta, as well as for deeper vaginal examination in the presence of an internal tear. A single narcosis secured in this manner, slowly, with a diluted gas mixture, is usually satisfactory.

CONTINUOUS NARCOSIS

This should be attemtped only by a competent anesthetist. Its necessity in ordinary labor is rare, and its greatest usefulness applies in major obstetric operations.

Occasionally it becomes useful in controlling the nervous patient, and it is applied as routine by some operators during the delivery period.

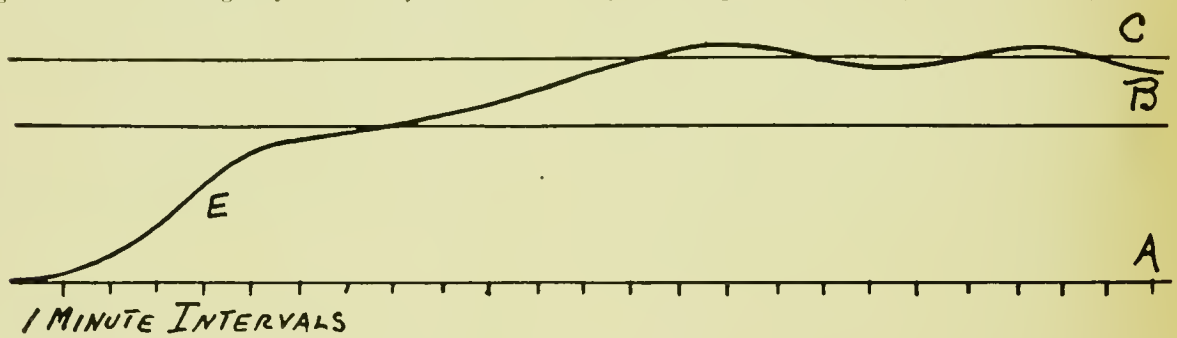


Chart 9. Continuous analgesia curve, illustrating the apparent progressive increase in depth, with the same gas mixture, continued over a long period of time.

The detailed technic for this state in obstetrics is the same as that in general surgery, and belonging as it does to the special anesthetist, it need not be discussed in this report.

REBREATHING

The principal advantage of rebreathing in this work is economy. In continuous analgesia or narcosis it serves to warm the gases, thus fortifying against the possibility of irritation of the upper respiratory passages. The character of results, the safety and comfort of the patient, do not seem to be unfavorably influenced by it.

As a rule about 50 per cent. of the entire volume of gas is rebreathed, but this must at times be decreased to meet special indications.

The refractive patient will usually respond better with a smaller rebreathing volume.

Retention of carbon dioxid, as accomplished by rebreathing in surgical narcosis, for the purpose of respiratory and cardiovascular stimulation in the mother, has never been indicated to my knowledge in obstetrics under the administration of nitrous oxid.

SELF-ADMINISTRATION METHOD

The safety which this method provides under all conditions is appealing. With it, the possibility of accident with any nitrous oxid mixture is inconceivable. It is productive of satisfactory results, and it renders unnecessary the inconvenience of calling an anesthetist for every normal labor.

This method lessens the necessity for absolute dosage. Lapses into narcosis, particularly after the first half hour, are more common, but these are so quiet that they often pass unnoticed and cause no inconvenience.

Self-administration is usually more satisfactory to the patient, and the fact that it gives the mother something to do during the labor is not without value.

APPARATUS

Any apparatus which will deliver to the patient an adjustable mixture of nitrous oxid and air, or oxygen, may be employed with satisfactory results. Success here depends, not so much upon the apparatus, as upon the way in which it is operated.

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SUFFERING DURING LABOR IS BUT THE TIDE IN THE OCEAN OF MOTHERHOOD AND THE DESIRE OF MOTHERS IS EUTOCIA—NOT AMNESIA. THE BELIEF THAT PAIN IS AN INEVITABLE ACCOMPANIMENT OF LABOR HAS RECONCILED MOTHERS TO ENDURE IT, WHILE THE JOY OF SUCCESSFUL MOTHERHOOD HAS CAUSED THEM TO FORGET IT. THERE IS, HOWEVER, NO LOGICAL REASON WHY WOMEN SHOULD SUFFER DURING LABOR.

—Carl Henry Davis.

ALKALOIDAL AMNESIA IN OBSTETRICS . HISTORICAL REVIEW . ETHER . CHLOROFORM A LA REINE . MORPHIN-SCOPOLAMIN . PANTOPON . HEROIN . TOCANALGIN . TECHNIC OF ADMINISTRATION . ADVANTAGES AND DISADVANTAGES . LIMITATION OF UTILITY . COMBINED NARCOSIS IN NORMAL LABOR AND OBSTETRICAL OPERATIONS

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AMONG THE MANY contributions to surgery, none has exerted a more beneficial influence towards its improvement and progress than the introduction of anesthesia for the relief of pain incident to operative procedures. No less important, at least, from the obstetricians point of view, has been the application of anesthesia to the ordeal of childbirth. Sir James Y. Simpson, as early as 1847, speaking in defense of painless labor, said that *"pain in excess is destructive, and even ultimately fatal, and the great pain accompanying parturition is no exception to this general pathological law."*

If this be true, is it not demanded that we shall employ those means at our comand for the alleviation of pain incident to childbirth?

In former years many reasons were advanced, by laymen, physicians and clergy against the unnecessary employment of such agents and even today there are those among us who deny the necessity of ameliorating the pain of childbirth. But notwithstanding this opposition during the past seventy years, many drugs have been used for this purpose, each of which has had its supporters, but the ideal agent is at present unknown.

HISTORICAL CONSIDERATIONS

Of the many drugs employed as anesthetics or analgesics during labor, ether was the first. Sir James Y Simpson who early recognized the advantages of an anesthetic in major surgery, could see no reason why the pain of parturition could not be lessed or even abolished by anesthesia without interfering with the natural course of labor. This he accomplished in January, 1847, when he confined the first woman ever delivered under the influence of an anesthetic.

In November of the same year, he began the use of chloroform in obstetric practice, and from the year 1853 when it was administered to the Queen of England, *Chloroform a la reine* has remained, even to the present day, the universal agent for the relief of pain during the later stages of labor.

Besides Simpson in Edinburgh, Dubois and Deschamp, of Paris, wrote in 1847 about the use of ether anesthesia in labor. During the same year Morton and Keep, in Boston, employed ether inhalations during labor. Pajot, of Perrin, in 1854 wrote of the advantages of chloroform inhalations for the relief of pain during childbirth. While in 1878 Pinard wrote an elaborate monograph entitled: "The Comparative Action of Chloroform, Chloral, Opium and Morphin on Women in Labor," and many of his deductions still remain unquestioned. From his experience he concluded that chloral was of little value, and that while morphin was frequently useful, its results were not so satisfactory as those of chloroform. Chloral stopped the labor every time; morphin only occasionally.

Paul Bert in 1878, recommended nitrous oxid, if given with oxygen, for long anesthesia, but it remained for Klikowitch, of Petrograd, in 1880, to demonstrate its efficacy for the mitigation of pain incident to labor. Döederlein, in 1886, refers to the use of nitrous

oxid and oxygen in obstetrics, but he only employed it to obtain surgical anesthesia. This method of anesthesia then apparently disappeared from general use until Webster, of Chicago, in 1905, used nitrous oxid and oxygen to obtain surgical narcosis in certain abnormal obstetric cases, notably Cesarian Section. Later Webster and his associate Lynch, of Chicago, and Guedel, of Indianapolis, began to use nitrous oxid and oxygen as a routine measure for the relief of pain during labor, to produce analgesia or obstetrical anesthesia. (See A. E. Guedel: Nitrous Oxid in Obstetrics: herewith printed in the Year-Book.)

In 1885 cocain in solutions of varying strength was applied to the cervix and external genitals by Doleris and others in France for the purpose of lessening labor pains. In the same year, Tuffier and Malartic used cocain and later stovain, intraspinally for the relief of pain during childbirth. These methods proved unsatisfactory, for aside from the danger of the drugs themselves, the analgesia only lasted from one to one and a half hours.

In 1902 Schneiderlein, and in 1903 Steinbuchel, began to employ morphin-scopolamin for anesthesia in obstetrics. Since these men published the reports of their work, there has been more or less activity in this field. In 1906 Krönig and Gauss reported their first series of 500 cases of morphin-scopolamin analgesia and from that time the method has been the subject of discussion and investigation in all parts of the world, particularly in America during the past year.

Other agents which have shared in the universal efforts of the profession to lessen the pain of labor, are *pantopon*, first used by Jaeger or Kiel, in 1910; *heroin* first used by Kapp, of San Jose, California, in 1912; and finally *tocanalgin*—morphineless morphin—introduced by Prof. Dessaignes, of Paris, in 1914.

ETHER AND CHLOROFORM

When ether and chloroform were introduced into obstetric practice by Sir James Y. Simpson, of Edinburg, in 1847, they were administered only during the passage of the head over the perineum or for the application of forceps or other obstetric maneuvers. Their safety was insured because of the small amount of anesthetic given. In fact, only analgesia, with perhaps a certain degree of amnesia, obstetric anesthesia, was attained. Rarely surgical anesthesia, total obliteration of consciousness, was employed for the more difficult obstetric operations. Following this limited use of ether and chloroform, there came a time when there seemed to be no limitation to the use of these agents, for *Chloroform a la reine* was given by Snow for 31 hours; by Prothero Smith for 28 hours; and by Simpson for 14 hours, without endangering the life of the mother or child. However, in more recent years, since the action of ether and particularly that of chloroform, upon the various excretory organs, especially the liver and kidneys, has been better understood, the use of these agents has gradually become restricted to the latter part of the second stage of labor. Furthermore, it has been conclusively demonstrated that chloroform and ether anesthesia predispose to postpartum hemorrhage. Graham, has shown that the placental transmission of chloroform plays an important role in the causation of hemorrhagic diseases of the newborn. (See A. E. Graham: Late Chloroform Poisoning: herewith printed in the Year-Book.) Again prolonged anesthesia or too deep surgical anesthesia endangers the life of the child in direct proportion as the mother's life is jeopardized, and is, therefore, not without considerable danger to the child in a certain percentage of the more complicated cases. The technic of the administration of ether and chloroform is simple. Ether given to the desired stage of anesthesia by the *drop method* is the ideal form of administration. When given in this manner, ether may be begun when the head is bulging the perineum and continued throughout the remainder of the second stage of labor. Chloroform may be given for a much longer period of time, for by keen judgment, analgesia may be established with the crescendo of each pain, the patient immediately regaining full consciousness. This procedure is repeated with the beginning of each uterine contraction. Given in this manner, *Chloroform a la reine* may be administered with apparently perfect safety for from one to three hours.

As Dr. Guedel deals with the subject of

nitrous oxid and oxygen in obstetrics, it is not necessary to duplicate his discussion.

MORPHIN-SCOPOLAMIN.

Morphin with scopolamin was first introduced into obstetrics by Scheiderlein in 1902, and developed by Von Steinbüchel in 1903. It was subsequently used by Krönig, Pankow and Gauss with varying success. The advantages of morphin-scopolamin amnesia as recognized today are, that in a labor already established, amnesia can be continued throughout the first stage without interfering with or prolonging the labor. Morphin and scopolamin are distinctively first stage drugs, and while they have no effect in lengthening the first stage, they do definitely increase the duration of the second, and increase the danger of foetal asphyxia if the second stage is allowed to continue too long. To the mother, moderate use of either drug has no serious effect. They tend to diminish the shock of labor and favor speedy convalescence. Their employment should be limited to the first stage, after labor is definitely established. They should never be used when there is a question of a dead child, in primary uterine inertia, or in the presence of the accidents of pregnancy or labor. It is perhaps in heart diseases and tuberculosis that the greatest benefit will be derived from the use of these drugs in labor. The technic is simple but demands that the administration be under the guidance of a trained operator. The patient should be placed in a room by herself, the room darkened, her ears plugged and her eyes bandaged, and when the pains are strong and regular, recurring at five minute intervals, and the cervix is the size of a 25 cent piece, the first dose is given, using a 1-4 grain of morphin and a 1-130 grain of hydrobromid scopolamin Roche. One hour later the patient is given 1-200 grain of hydrobromid of scopolamin, and one hour later 1-400 grain. If the amnesia is complete, as it usually is by the third dose, as shown by the patient's lack of recollection of the previous needle punctures, the scopolamin may be repeated at from two to four hour intervals, in 1-400 grain doses. The foetal heart must be constantly watched, particularly in the second stage as narcotized infants bear the trauma of labor badly.

PANTOPON.

Sahli, of Berne, discovered pantopon in 1909 and recommended its use instead of opium and its derivatives. It is a mixture of the soluble chlorides of opium and is freely soluble in water. It contains 89.77 per cent. of all the alkaloids of opium and is about five times as active. The average dose of pantopon is 1-6 to 1-3 grain.

Jaeger, of Kiel, in 1910, first used pantopon for the purpose of allaying the pain of parturition. He reported 50 labors, 20 in which pantopon alone was used, and 30 in which pontopon and scopolamin in combination were given. The dose given in these cases was one injection of a 0.5 to 1.0 cc. of a 2 per cent. solution of the drug, 1-6 to 1-3 grain either alone or in combination with 1-200 to 1-150 grain of scopolamin. Jaeger observed that when given alone pantopon only decreased sensitiveness of the labor pains, while in combination with scopolamin it produced a *twilight sleep* with complete analgesia and amnesia.

Jaeger, along with Aulhorn, Kolde, Zeller, Esch and others recommend the administration of pantopon as soon as the pains have become strong and recur at regular intervals. Morley, of Detroit, however believes it is best given with the beginning of the second stage of labor.

The most noteworthy advantage in the use of pontopon lies in the fact that it is absolutely harmless to the child. Other advantages that deserve mention are;

(1) It is freely soluble in water and is not irritating to the subcutaneous tissues.

(2) In combination with scopolamin it produces complete analgesia and amnesia in from 60 to 70 per cent. of cases.

(3) It has no unpleasant after-effects to mother or child.

(4) It can be used at the home or in the hospital with equal safety.

From a study of the published reports on the use of pantopon in obstetrics, there appears to be no danger from its use, except when given in very large doses, 2-3 grain, or more. In such doses the child may be born in a state of apnoea, but can invariably be made to breathe within a few minutes.

Pantopon may be used in every case of labor not presenting grave complications. Accord-

ing to Esch, it should not be used in cases of primary uterine inertia or when quick delivery is desired. It should be used with caution in lung complictions, disturbances of the circulation, general and febrile diseases, chronic kidney disease, syphilis, and premature deliveries.

The mode of administration is by hypodermic injection. One cubic centimetre of a 2 per cent. solution, 1-3 grain, should be given as the initial dose. From one to three injections may be given. Usually one injection is sufficient to produce analgesia, particularly when used in combination witth 1-150 grain of scopolamin. The desired effect is obtained in from 20 to 30 minutes and lasts from 1 1-2 to 2 hours or longer. Esch has recommended much smaller doses of pantopon and scopolamin, but repeats the injections more frequently, each time using a smaller dose of the drugs. The results are apparently no better than by the older methods of giving larger doses.

HEROIN.

Kapp, of San Jose, California, in November, 1914, reported about 100 cases of labor in which he used heroin hydrochlorate to lessen the pains.

Moderate analgesia, without amnesia, is the object of this form of treatment. Between pains the patient sleeps lightly but can be easily aroused. When awakened she is perfectly rational but immediately falls asleep again.

The chief advantages claimed for this method of producing *painless labor* are:

(1) The family physician can use it with perfect safety in the home.

(2) The second stage of labor is shortened, because due to the lack of pain, the patient uses her expulsive forces to better advantage.

(3) It reduces postpartum shock by giving the mother a few hours sleep following the labor.

(4) It does not predispose to postpartum hemorrhage.

(5) It is absolutely harmless to the baby.

In the experience of the authors, there is no danger in the use of heroin either to mother or child. We recommend the drug unreservedly for all uncomplicated cases of labor.

The first injection of 1-12 grain is given when the pains are strong and recur at regular intervals. Within 20 minutes the patient becomes drowsy and *no longer feels the sting of the pains.* The initial dose is effective for from 2 to 3 hours. Repeat doses of from 1-24 to 1-36 grain may be given whenever needed—when the patient feels pain. Rarely more than one or two doses are needed.

TOCANALGIN

Tocanalgin, the so-called *morphinless-morphin,* is a substance obtained by the action of certain living ferments on the chlorhydrate of morphin. It is therefore a hydration product of morphin but exhibits none of the characteristics of morphin. Its toxicity is about 1-15 that of ordinary morphin, and hence is vastly safer. It was first isolated by Paulin, a French chemist, who recommended it as a substitute for morphin, maintaining that its power to produce analgesia and amnesia was in every respect equal to that of morphin.

Prof. Ribemont Dessaignes, of the French Academy of Medicine, was the first to use this new drug, tocanalgin, in obstetrics. In July, 1914, he reported 112 labors in which this agent was used to produce analgesia or amnesia. Seventy-five per cent. of the 112 cases had complete analgesia, 22 per cent. showed partial analgesia, and 3 per cent. were not in any way affected by the drug.

There were 115 babies, 77 of which cried spontaneously; 28 were born in a state of apnœa but cried in a few moments; one was born dead but the fœtal heart could not be heard previous to the administration of the drug. The remaining 9 were more or less asphyxiated when born, but after respiration was established, they progressed as normal babies.

The advantages claimed for tocanalgin are:

(1) Its lessened toxicity as compared to morphin.

(2) It has no effect upon the uterine contractions.

(3) The temperature and pulse remain normal following its administration.

(4) Lactation is not interfered with.

(5) Involution is normal.

(6) It does not predispose to postpartum hemorrhage.

(7) Versions, forceps and perineal repairs do not require further anesthesia.

(8) Seventy-five per cent. of the labors are rendered painless, with no after effects to the mother.

The dangers of tocanalgin is chiefly for the baby. Notwithstanding the fact that it is 1-15 as toxic as morphin, yet is is toxic enough to produce oligopnœa in a certain per cent. of babies. Furthermore, it prolongs the second stage of labor, but just how much it is not definitely stated.

The method is applicable to all normal cases of labor but should not be employed where there is any likelihood of complications.

Tocanalgin may be given when the uterine contractions are strong and recur at regular intervals—the cervix two or more fingers dilated, or at any time during the second stage of labor. Unlike morphin and scopolamin, it may with safety be given only a few minutes before the birth of the child.

The dose for the first injection is 1 1-2 cc. For subsequent injections, 1-2 to 3-4 cc. is the usual dose. Repeat doses may be given whenever the uterine contractions become painful. From one to three injections may be given. Usually one is sufficient.

MUCH OF THE INCREASE OF MATERNAL MORTALITY WILL BE FOUND IN THE MISUSE OF ANESTHESIA AND IN THE RIDICULOUS PARODY WHICH, IN MANY PRACTITIONERS' HANDS, STANDS FOR THE USE OF ANTISEPTICS. IN A WORD, THE USE WHICH HAS BEEN MADE BY MANY OF TWO OF THE GREATEST BLESSINGS OF HUMANITY, HAS CONVERTED THEM INTO LITTLE ELSE THAN A CURSE. BEFORE THE DAYS OF ANESTHESIA INTERFERENCE WAS LIMITED AND OBSTETRIC OPERATIONS WERE AT A MINIMUM, BECAUSE INTERFERENCE OF ALL KINDS INCREASED THE CONSCIOUS SUFFERING OF THE PATIENT. WHEN ANESTHESIA BECAME POSSIBLE AND INTERFERENCE BECAME MORE FREQUENT, BECAUSE IT INVOLVED NO ADDITIONAL SUFFERING, OPERATIONS WERE UNDERTAKEN WHEN REALLY UNNECESSARY, ON THE DEMAND OF THE PATIENT OR FOR THE CONVENIENCE OF THE PRACTITIONER. AND SO COMPLICATIONS AROSE AND THE DANGERS OF LABOR INCREASED. BUT THE KNOWLEDGE THAT THIS INTERFERENCE INVOLVED RISKS MUST HAVE SERVED AS A SALUTARY CHECK TO SOME EXTENT.

WHEN THE PRACTICAL OBSTETRICIAN REALIZES HIS RESPONSIBILITY, AND THAT NO SMALL SHARE OF THIS TERRIBLE MATERNAL MORTALITY OF A CERTAINTY LIES AT HIS DOOR, HE HAS MADE THE FIRST STEP TOWARD TRUE PROGRESS. WHEN HE REALIZES THAT LABOR IS A NATURAL PROCESS, WHICH IN THE GREAT MAJORITY OF CASES IT IS CRIMINAL TO DISTURB ; WHEN HE REALIZES THAT EVERY INTERFERENCE INCREASES THE INHERENT DANGERS A HUNDRED-FOLD ; AND WHEN UNDER THIS CONSCIOUSNESS HE BRINGS WITH HIM TO THE LYING-IN ROOM ALL THAT IS POSSIBLE OF THOSE PRINCIPLES OF ANTISEPTIC SURGERY WHICH HAVE BEEN AT THE BOTTOM OF THE TRIUMPHS OF MODERN GYNECOLOGY, WE SHALL NOT HAVE LONG TO WAIT FOR THE LIGHTENING OF THE DARK CLOUD WHICH HANGS OVER US NOW.

—*Milne Murray.*

THE NASAL ADMINISTRATION OF NITROUS OXID-OXYGEN ANESTHESIA AND ANALGESIA . RESEARCHES OF KARL CONNELL ON THE ACTION OF NITROUS OXID-OXYGEN AND ITS ZONES OF ANESTHESIA AND ANALGESIA . PRELIMINARY MEDICATION AND ACCESSORY NARCOSIS . PATHOLOGICAL CONDITIONS OF PATIENTS . QUALIFICATIONS OF THE SUCCESSFUL ADMINISTRATOR . TECHNIC OF ANALGESIA . TECHNIC OF ANESTHESIA . McKESSON'S CHART OF PHENOMENA UNDER NARCOSIS . ANOCI-ASSOCIATION . HANDLING EMERGENCIES.

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UNFORTUNATELY THE INITIAL revival of interest in nitrous oxid anesthesia and analgesia was wrecked by the stubborn ignorance of many administrators who thought that an automatic apparatus solved all the problems of administration and who were too slothful to study the theory and practice of narcosis.

The present recrudescence of interest, however, is established on the firm foundation of scientific research and clinical achievement; and while the educational facilities for acquiring expert knowledge of nitrous oxid anesthesia and analgesia are not yet what they should be, earnest efforts are being made to offer courses and clinical instruction in these subjects that will enable those who desire to fit themselves as competent anesthetists.

Local anesthesia is suffering from the same misguided enthusiasm on the part of its advocates that imperiled the stability of nitrous oxid anesthesia and analgesia as routine methods of narcosis. Presently local anesthesia will find its true field of utility in surgery, the specialties and dentistry; and while these distinctive methods of relieving pain have their indications and contraindications for specific procedures, and in individual cases, their combined usefulness in the technic of anoci-association is being more and more widely recognized.

Quite the greatest advance in surgical procedure since the discovery of anesthesia has been the working out of the scientific control of the narcotic state through the development of the nonasphyxial method of nitrous oxid administration, originally suggested by Andrews, of Chicago, experimented with by Paul Bert, of France, and Hillischer, of Vienna, and later perfected by Sir Frederic Hewitt, of London. Anesthesia transformed surgery from a shambles with an excessive mortality to a painless beneficence with a negligible morbidity. The nonasphyxial method of narcosis with its accurate control of the zones of anesthesia and analgesia, has practically eliminated anesthetic and surgical mortality, and at the same time opened new realms of conquest to the operator. Nonasphyxial analgesia has extended this painless beneficence to many minor procedures, not serious enough to require profound narcosis, but too painful, too nerve-racking to be borne by the average patient without unbearable discomfort or serious risk.

Of the general anesthetics in common use nitrous oxid is not only the safest, so far as the ultimate risk of life is concerned, but also the least harmful in its immediate effects upon metabolism. Recovery, after its administration, is decidedly prompt and usually without postoperative complications such as retching, vomiting and toxhemia. Nitrous oxid is rapidly eliminated from the system and has, comparatively, a negligible effect upon the blood, tissues and organs of the body, all of which resume their normal function very shortly after the discontinuance of its administration.

The advantages of the nonasphyxial method of administration may be briefly summarized as follows:

The paramount safety of nitrous oxid (with proper mixtures of air and oxygen), as a general anesthetic agent, is an established proposition—the facts prove it. Its zones of anesthesia and analgesia are more accurately controllable than those of any other form of narcosis. During its nonasphyxial administration the operator has equally at his command the analgesic stage, in which the patient is conscious, but feels no pain, and profound narcosis, when every sense is stilled in letheon forgetfulness; and either stage can be prolonged indefinitely or readily transformed into the other without untoward complications.

Before proceeding to a consideration of the nasal method of administering nitrous oxid, it seems advisable to review some experimental researches that have been conducted recently to establish the intensity of the action of nitrous oxid and the zones of available anesthesia and analgesia resulting from its administration with varying admixtures of oxygen.

RESEARCHES OF KARL CONNELL ON THE ACTION OF NITROUS OXID AND ITS ZONES OF ANESTHESIA AND ANALGESIA, WHEN ADMINISTERED WITH OXYGEN

The intensity of the anesthetic action of nitrous oxid, is, in a measure, inversely as the quantity of oxygen with which it is administered. The effect varies from a blunting of the pain sense, obtained by administration with a percentage of oxygen exceeding that of normal air, down through increasing anesthetic action, obtained by a percentage of oxygen one-half that of the normal atmosphere; thence down through an increasingly anesthetic and asphyxial action until finally, with a percentage of oxygen about one-third that of normal air, the asphyxial effect renders the mixture so dangerous that it may be termed irrespirable. The effect of dosage may therefore be tabulated within certain limits, according to the relative percentage of the two gases maintained for respiration.

GAS TENSION AS A FACTOR

Additionally the anesthetic action of nitrous oxid is, in a measure, directly proportional to the tension of the gas dissolved in the blood and central nervous system. Indeed any appreciable dilution of the anesthetic mixture by an inert gas, such as nitrogen, so lowers the volumetric proportion of normal atmospheric pressure sustained by nitrous oxid in the lungs and results in such low gas tension of the nitrous oxid dissolved in the blood, that satisfactory anesthesia cannot be induced. In this connection the well recognized increased anesthetic efficiency of nitrous oxid, administered under a few millimeters of positive pressure can scarcely be cited as an illustration, since the clinical advantage accruing in this instance is no doubt due to the exclusion of air, which so often finds ingress into the apparatus through leaking joints or inhalers, rather than to additional nitrous oxid dissolved in the blood. It is difficult to imagine that 5 mm. of positive pressure would add an amount clinically appreciable to the 680 mm. of tension, more or less, of nitrous oxid in the central nervous system of the anesthetized patient.

AN ACCURATE STANDARD AVAILABLE FOR THE HYDROCARBON ANESTHETICS

With the lipoid solvent anesthetics, decreased oxygen supply is a secondary factor in the depth of anesthesia, the determining one being the actual vapor tension of such agents dissolved in the neuron. Therefore, with these anesthetics, ether and chloroform, it would seem desirable, as urged by Boothby, to adopt a nomenclature of dosage referring to the barometric pressure exerted by the vapor in the lung and the tension under which it has held dissolved in the neuron.

NITROUS OXID STANDARD OF QUALITATIVE DOSE

With nitrous oxid, on the other hand, since its efficiency is in larger measure proportional to the deprivation of oxygen, it seems desirable, until further work on the nitrous oxid tension of the blood has been done, to measure and tabulate dosage in terms of relative volumes of nitrous oxid to oxygen in the inspired tidal volume.

LIMITATION OF THE QUALITATIVE DOSE STANDARD FOR NITROUS OXID

It must be recognized that the proportion of gases in the tidal volume is only an approximate index of the proportion of available gases which reach the central nervous system. Oxygen is perishable in the body and must be constantly refreshed; whereas with nitrous oxid, no loss being sustained, a partial clinical balance of blood and neuron with alveolar gas is established within 6 minutes, and an almost complete balance within 15 minutes, and a complete physical balance within about 40 minutes, if analogy with carbon dioxid may be drawn. Therefore, after a time, it makes no difference with the amount of nitrous oxid circulating in the blood, what the tidal volume of respiration may be, so long as an equal gas pressure is maintained in the lungs. But for the oxygen of the blood to maintain a balance and the anesthetic state to remain in equilibrium, the oxygen intake in the tidal gas respiration must remain constant in quantity within certain limits, no matter what the percentage may be. In other words, the percentage of oxygen must be raised to compensate for small tidal volume, thus upsetting the tidal proportion standard of dosage.

A second factor to upset the accuracy of dosage guaged by the relative proportion of gases in the tidal volume is an altered capacity of the blood to transfer oxygen. Any diminished rate of blood flow or diminished oxygen carrying power in the hemoglobin must be compensated for by increase of oxygen relative gas pressure both in the tidal volume and the alveolar air for the nerve cell to remain in anesthetic equilibrium.

Clinically it is found that the requirement of individual patients toward higher percentage of oxygen in the tidal volume is common when there is present any marked diminution of the tidal volume or of quality or rate of blood flow. The tidal volume is often diminished by obstruction, by breath-holding, by acapnia or by overdosage.

The oxygen-carrying capacity of the blood is diminished by low hemoglobin content and by decreased rapidity of flow; by anemic and septic conditions; also the relative capacity for a higher percentage of oxy-

gen is evident in rapidly growing children and in patients of excessive or rapidly-increasing weight. The carrying capacity being in direct ratio to the rate and volume of the blood flow is lessened in asthenic states, such as old age, cardiac decompensation and conditions of disease. Any and all these factors must be compensated for by increase of oxygen in the mixture administered to the individual patient.

The only practical place to measure the relative proportion of gases is at the intake of the inspired volume, however much this measurement may leave to be desired. Yet in normal man of average tidal volume the effect of a given proportion of gases can be foretold to a nicety and in the exceptions previously noted, the proper level is quickly found. By the use of a measuring instrument of precision for the quantity of each gas as it flows to the patient, the administration for a given depth of anesthesia becomes almost a rule of thumb and an automatic procedure.

ZONES OF ANESTHESIA

If it is conceived for purpose of observation and tabulation that the various stages of nitrous oxid-oxygen anesthesia, from slight blunting of pain sense to profound asphyxia, may be plotted as on a surface into continuous areas, each marked by definite physical reactions and each induced and maintained by definite proportions of nitrous oxid and oxygen, then these areas may be termed *Zones of Anesthesia.*

ZONES OF NITROUS OXIDE-OXYGEN ANAESTHESIA IN NORMAL MAN WITHOUT SUPPLEMENTAL NARCOSIS

PERCENTAGE IN TIDAL GASES		ZONE	DEPTH OF ANAESTHESIA	DEGREE OF ASPHYXIA	DEGREE OF RELAXATION	COLOR	UTILITY
NITROUS OXIDE	OXYGEN						
100%	0%	LETHAL	COMPLETE	GREAT TO FATAL	TONIC & CLONIC SPASM	BLUE BLACK	EXTRACTION OF TEETH; INCISION OF ABSCESS (USE CONDEMNED)
97%	3%						
95%	5%	PROFOUND	COMPLETE	CONSIDERABLE (DANGEROUS)	ASPHYXIAL RIGIDITY	DEEP CYANOSIS	
94%	6%	DEEP	COMPLETE	PARTIAL (DANGEROUS)	PARTIAL	MODERATE CYANOSIS	
92%	8%	MEDIUM	COMPLETE	PARTIAL	PARTIAL	SLIGHT CYANOSIS	INDUCTION
89%	11%	LIGHT	PARTIAL	SLIGHT	SLIGHT	FAINT CYANOSIS	ABDOMINAL SURGERY
86%	14%	VERY LIGHT	PARTIAL	0	0	NORMAL	SURFACE SURGERY (OR ABDOMINAL SURGERY WITH SUPPLEMENTAL NARCOSIS)
84%	16%	SUB CONSCIOUS	PARTIAL COMPLETE ANALGESIA	0	0	NORMAL TO PINK	
80%	20%	LIGHT SUB CONSCIOUS ANALGESIA	ANALGESIA	0	0	PINK	
50%	50%	CONSCIOUS ANALGESIA	EQUAL PARTS OF AIR ALLOWED			NORMAL	DENTISTRY

Chart 1. Connell's tabulation of the Zones of Anesthesia and Analgesia.

The accompanying chart has been tabulated as the average for normal man of good tidal volume. The mixtures and measurements were made by the Connell instantaneous gas flow guages. For guidance in tabulating the slightly asphyxial zones the author is indebted to Boothby, of Boston, for the analgesic zones to Teter, of Cleveland; while the profound asphyxial zones were determined in part by Gwathmey and myself on the dog. The remaining zones were tabulated from operative cases under routine anesthesia at the Roosevelt Hospital, New York City. These zones were determined without supplemental narcosis. It may be mentioned in passing that without supplemental narcosis for resistant subjects, no zone exists in the range of true nitrous oxid-oxygen anesthesia which is surgically desirable.

UTILITY OF ESTABLISHED ZONES

The Lethal Zone: Equilibrium can never be said to be established in this zone, as fatal asphyxia supervenes in from 3 to 6 minutes. While the percentages in this zone are in common use for short operations, such as the extraction of teeth, yet the asphyxial mixtures of this zone should be abandoned for those which induce anesthesia more slowly and safely. Anesthesia induced by the percentage mixtures of the lethal zone subject the patient to sever cardiovascular strain, and carry him to within a minute or two of death from asphyxia.

The Profound and Deep Zones: These have no proper surgical indication. They are frequently invaded by error during the routine administration and are rapidly retreated from by raising the percentage of oxygen when oncoming asphyxia is observed. By intratracheal insufflation of the mixture, a dog may be kept in the profound zone, alive, for half an hour. Man may be carried in the deep zone if the tidal volume be large and no asphyxial obstruction or thoracic fixation presents, yet the margin of safety is small.

The Medium Zone: The percentage of mixture even in this zone is advisable only for the first few minutes of induction, as the zone yields an undesirable degree of asphyxia characterized by a slight cyanosis, occasionally muscular rigidity, by stertor, and by cardiovascular strain. Some anesthetists utilize the physiologically disadvantageous asphyxia of this zone erroneously for additional degree of relaxation in resistant subjects. Relaxation cannot be secured in this zone in resistant subjects, but can only be secured by raising the percentage of oxygen and by supplemental narcosis; such narcosis as is attained by a small addition of ether.

The Light Zone: This is the one of greatest utility for abdominal surgery. The perfect relaxation of the hydrocarbon anesthetics is never present. Reflex muscular and respiratory reaction to trauma is always evident, unless blocked by local analgesia or by a more effective general anesthetic, such as small doses of ether, or a large preliminary dose of morphin.

The Very Light Zone: This is the desirable one for surface surgery, such as amputation of the breast. Both this and the subconscious zone may serve for all degrees of operative work when supplemented with ether. In fact these are the ideal zones, physiologically, since in these zones the blood pressure is not raised, the color is normal or even rose pink; the breathing is not exaggerated and there is no asphyxia present.

On the usual volume of from 8 to 10 liters of gases per minute, the percentage of oxygen in the gases delivered must be about 2 per cent. more than that charted in the accompanying table. On account of dilution with expired gases from which the oxygen has been in part absorbed. In patients, who are anemic or toxic from disease, or whose respiratory volume is small, or who have diminished blood flow, a higher percentage of oxygen is required to maintain the same oxygenation of the tissues. The percentages of oxygen needed in the inspired gases is approximately in direct ratio to the degree of anemia, or toxhemia present. For example, a patient with 50 per cent. hemoglobin or one-half the normal oxygen carrying capacity, requires for the zone of light anesthesia, 18 to 20 per cent. of oxygen in the tidal volume of respiration, instead of the 11 per cent. mixture required by normal man.

The stimulus of operative trauma elevates the blood pressure 10 to 30 mm. in all zones, even in the zone of profound anesthetic asphyxiation. Nitrous oxid has not the slowly induced ether effect in blocking efferent sensations of the somatic nerves by direct action on the nerve endings. Nor does it compare in efficiency as to central nerve cell disassociation with full ether anesthesia. The maximum nitrous oxid effect is about equivalent to the ether effect obtained by 30 mm. of

ether tension. Whereas full anesthesia under ether with complete disassociation of all the central nervous system, from the great primitive medullary centers, is accomplished by from 50 to 52 mm. of ether tension in the central nervous system, as has been shown in the anesthetic tension investigations of Boothby. Nitrous oxid should therefore be employed only with the gentlest manipulation of tissue by the operator, or where there is supplemental blockage of centripetal stimuli by local anesthesia or by a more effective general anesthetic, such as ether, or deep narcosis by morphin or scopolamin.

Figure 2. Showing the method of seating the patient in the chair; the adjustment of the nasal inhaler; connection of the apparatus directly to the chair, and source of gas-oxygen supply from the large tanks.

QUANTITATIVE DOSAGE

A consideration of dosage would be incomplete where a large avenue of excretion has been utilized and in part blocked, were not also the refreshing of the dose considered. In practice it is found that a refreshing of the gas at a rate about equivalent in bulk to the normal tidal volume suffices. I have never observed any ill effects from exceeding this rate, such as are alleged to arise from an over excretion of carbon dioxid. Excessive volume, however, is a monetary waste. A satisfactory level of anesthesia cannot be maintained unless the gaseous excrements such as carbon dioxid, are washed out at a comparatively normal rate. No smoothness of anesthesia can be maintained on less than 6 liters, and, in fact, 8 liters per minute, (120 gallons per hour), should be placed as the minimal delivery, or to active individuals 10 liters per minute. With the nitrous oxid flowing at the rate of 8 liters per minute, the oxygen is set at 3-4 liter per minute for induction. As soon as slight cyanosis appears the oxygen is raised to 1 liter and in about 5 minutes to 1 1-4 liters. After 15 minutes it can usually be raised to 1 1-2 liters per minute. If the patient is one re-

quiring larger percentage of oxygen in the tidal air to establish anesthesia in the proper zone, this fact is promptly evident and the oxygen is increased. Rarely are more than 2 liters of oxygen per minute required.

These researches of Connell not only establish the proper zones of anesthesia and analgesia for contemplated operative procedures; but they also indicate the quantitative admixture of oxygen required, and call especial attention to the use of supplemental etherization and alkaloidal narcosis in major surgery and to the necessity of preparing patients with sedatives or opiates for operative ordeals in minor surgery or dentistry.

Figure 3. Close-up view of the S. S. White nasal inhaler adjusted for use.

PRELIMINARY MEDICATION AND ACCESSORY NARCOSIS

In all cases in which pain, caused by the operative manipulation, is responsible for the patient's dread, nitrous oxid-oxygen analgesia is marvelously efficient. Salzer, of Cincinnati, however, points out the utter futility of attempting analgesia with nitrous oxid-oxygen alone, in patients who are excessively nervous and do not want to be conscious of what is going on. Until they have been educated to the efficiency of analgesia by several satisfactory experiences, they should receive some preliminary medication. Similarly the failure to use alkaloidal narcosis in conjunction with nitrous oxid-oxygen anesthesia or supplemental etherization when required either by resistant subjects or for proper muscular relaxation, merely serves to bring this method of anesthesia into disrepute.

While even difficult subjects will withstand operative procedures under anesthesia and analgesia remarkably well, when properly fortified with sedatives, even the most callous patients should receive the benefit of combined alkaloidal narcosis previous to prolonged procedures under nitrous oxid-oxygen. The proper use of sedatives or opiates will not only prevent collapse on the table or in the chair, but will also obviate delayed shock, which

otherwise may occur several days after operation.

Sedatives or opiates should be routinely employed previous to anesthesia and analgesia, unless specifically contraindicated by the patient's condition or the fact that their use may precipitate or exaccerbate *acidosis*. Judiciously administered they undoubtedly control the incidence of *psychic shock*, of which there is a great deal more in our surgical clinics and dental offices than we are inclined to credit.

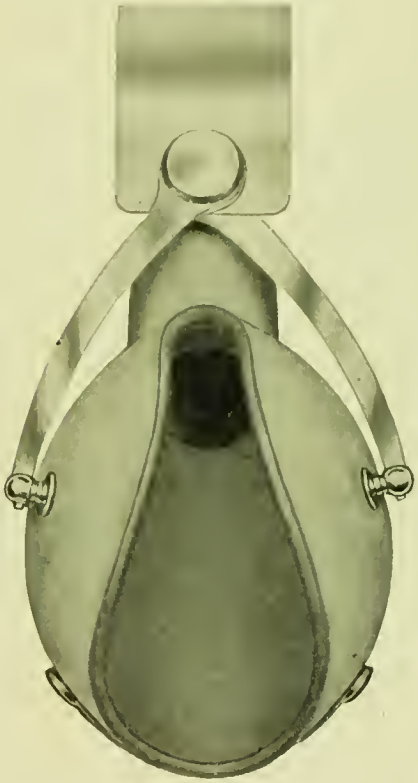

Figure 4. The S. S. White nasal inhaler adjusted for a long slender face.

Physicians, surgeons, specialists, anesthetists and dentists should one and all accord their patients the same comforts and protection which they are such sticklers in demanding for themselves when operated on under anesthesia or analgesia.

Among the sedatives conspicuously vailable for preparing patients for analgesia and promoting their comfort after operation are the triple bromides (effervescent), bromural and trigemin. Paraldehyd is useful in handling drug habitues, and Barber, of Chicago, has found adalin and strychnia of great service in the temporary control of alcoholism. It is futile to attempt the reformation of such types of patients just previous to anesthesia or analgesia. They must be tided through the anesthetic and operative ordeal as extrahazardous risks.

When opiates are necessary for combined narcosis or the control of severe after-pain, or the strain incident to prolonged procedures, codia and the coal tar analgesics are preferable to morphin. Dionin is comparatively free

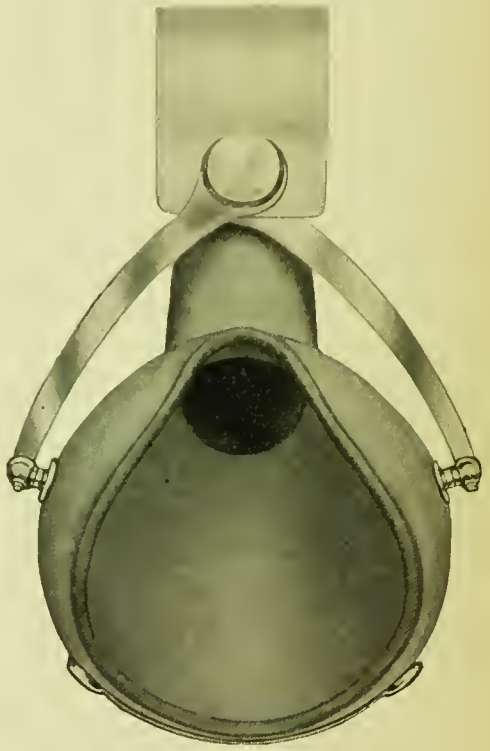

Figure 5. Adjusted for a fat, broad face.

from the nauseating propensities of morphin, and a combination of morphin, hyoscin and cactoid (Abbott) is ideal when alkaloidal narcosis is positively indicated. This combination cuts down the morphin dosage at least one-half, while the hyoscin controls the secretions of mucous membranes, thereby materially aiding the anesthetist and operator with a dry operative field, especially in the mouth and throat. While the use of opiates is occasionally absolutely contraindicated, still McKesson has used morphin (1-10 to 1-4 gr.) and hyoscin (1-300 to 1-100 gr.) in variable dosage,

depending on the age, size, temperament and condition of patients, in 5,000 cases without untoward effect, aside from infrequent nausea of short duration, which disadvantage has been decidedly offset by the mental quietude of the patients and their freedom from shock and after-pain.

PATHOLOGICAL CONDITIONS OF PATIENTS AS AFFECTING NITROUS OXID-OXYGEN ANESTHESIA OR ANALGESIA

Progressive members of the allied professions are gradually, however slowly, coming to

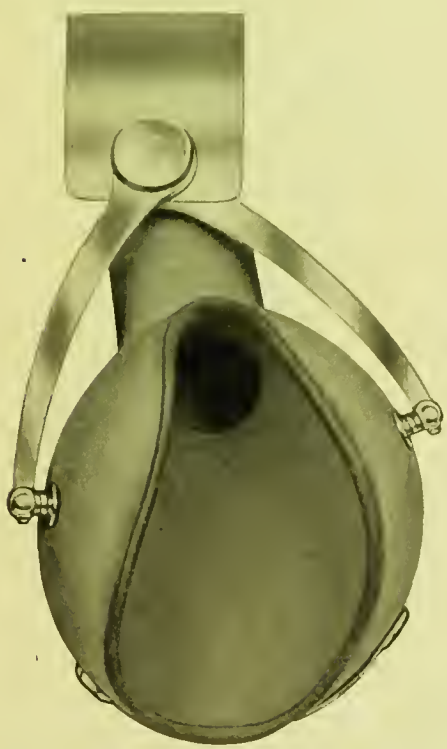

Figure 6. Adjusted for tumefaction of one side of the face.

the realization that neurasthenia, hysteria and abject emotional fear are almost invariably associated with endo- or myocardial degenerations from toxhemia. While nitrous oxid-oxygen is not essentially more dangerous when administered to such patients, than are the hydrocarbon anesthetics, these patients will collapse and die suddenly under the ordinary conditions of life and consequently are extra-hazardous risks. Of the same type are patients with exopthalmic goitre. Uncompensated heart lesions are an absolute contraindication to anesthesia or analgesia. Valvular lesions with established compensation withstand anesthesia and analgesia remarkably well, providing fluctuations in blood pressure are obviated, trauma is reduced to a minimum and hemorrhage is rigidly controlled.

Fortunately the majority of patients presenting with a personal diagnosis of *heart trouble* are usually the victims of prolonged gaseous indigestion. These patients may develop a pseudoangina under anesthesia or analgesia, and should receive preliminary treat-

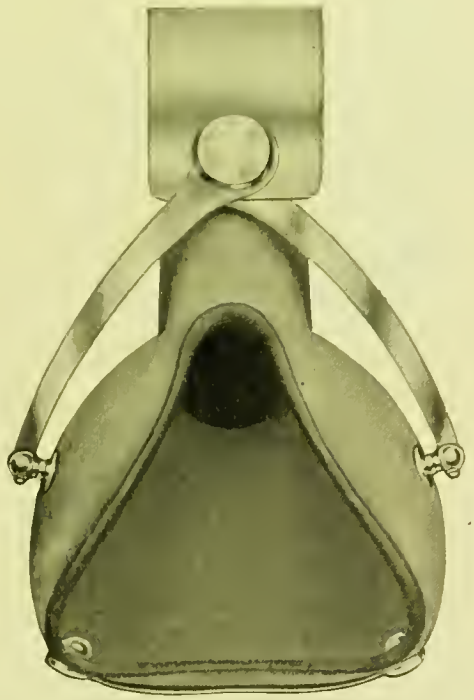

Figure 7. Adjusted to secure increased freedom in working on the upper teeth.

ment with laxatives, proper diet and antacids such as milk of magnesia, until their indigestion is sufficiently under control not to produce untoward complications. Alcoholics, tobacco and drug addicts have to be accepted and operated on as such. It is important, however, not to confuse these conditions with heart and circulatory disturbances due to organic disease.

Occasionally patients present with a bad anesthetic history. Aside from alcoholism and drug addiction these types of patients usually

have uncompensated heart lesions or are subjects of anginal attacks. Patients with uncompensated heart lesions give a history of collapse, during or after anesthesia or analgesia, necessitating a prolonged period of resuscitation. The condition may be suspicioned by the evidence of purple lips, and finger nails and various grades of dyspnea. On the contrary patients subject to anginal attacks are of the nervous type and give a history of being unable to *go-under* an anesthetic. The condition is usually diagnosed after unsuccessful anesthesia. A pertinent case report may be of interest:

ILLUSTRATIVE CASE:—Mrs. M., aged 35; came to operation in Dr. Hinckley's service at St. Mary's Hospital, Cincinnati, O., for removal of a small warty growth on the labia minora. Chloroform was the routine anesthetic of this clinic. The patient had scarcely taken half a dozen whiffs of chloroform when she went into a clonic spasm, during which the radial artery felt like

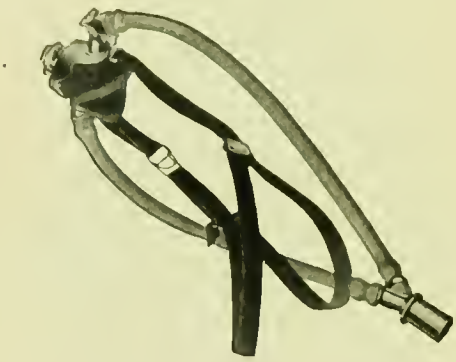

Figure 8. Teter nasal inhaler, showing double supply tubes and adjusting harness.

an e string on a violin and the pulse rate fell to from 4 to 6 a minute. Amyl nitrate 5 mins. was given immediately by inhalation. Ether was substituted and a 500 gramme can exhausted by the closed-cone method before the circulation and musculature relaxed sufficiently for anesthetic absorption. No cyanosis presented at any time. The operation was performed with the patient in a state of ether-analgesia and still muttering incoherently. She never became really anesthetized. Later the patient gave a detailed history of two similar experiences at other hospitals, in which the anesthesia was so unsatisfactory that the operation could not be performed. Fortunately such attacks of angina pectoris complicating anesthesia are extremely rare.

Pregnancy is no contraindication to nitrous oxid-oxygen anesthesia or analgesia. The recent, extensive use of nitrous oxid in obstetrics is proving rather conclusively that this agent has no effect on the muscular action of the uterus nor any dilaterious effects on the unborn child. Nauseau and vomiting after anesthesia or analgesia should, of course, be avoided for obvious reasons.

On the contrary it is inadvisable to administer nitrous oxid-oxygen during *menstruation,* if for no other reason than that the sexual centers are stimulated at this time and erotic sensations and hallucinations may result, thus placing the administrator in a very disagreeable position.

Figure 9. Teter naso-pharyngeal tubes with pressure regulated expiratory valve.

Unless operation is absolutely imperative, it is inadvisable to administer nitrous oxid-oxygen if the condition of the air-passages is such that septic material may be forced into the *sinuses* or inspirated into the trachea or lungs. Acute coryza, epidemic grippe and streptococcic sore throat all contraindicate anesthesia or analgesia and operative procedures, until their virulence has been effectively moderated by proper treatment. The toxemia of grippe has a peculiar affinity for

the heart and patients suffering from this prevalent complaint, may readily collapse, if subjected to anesthesia or analgesia even during convalescence.

While hemorrhage during and after operative procedures under nitrous oxid-oxygen anesthesia or analgesia may be controlled by the surgeon or dentist by ligation, suture or packing, there is a class of patients in whom these methods of control do not always avail. *Hemophiliacs* or easy bleeders are extremely disconcerting risks, but fortunately the researches of Kocher and Fonio have at length provided a remedy that is almost specific for hemorrhage in these peculiarly constituted individuals. It consists of the isolated dried fibrin element of blood and is marketed as

Figure 10. The A. C. Clark nasal inhaler for the self-administration method. The trigger-valve enables the patient to control the supply of gases.

coagulen or coagulose, and when dissolved and injected subcutaneously or used locally as a hemostatic powder, it not only controls persistent bleeding or oozing, but also lacks the anaphylactic propensities of horse serum. Injections of coagulose should always be supplemented with intramuscular injections of pituitrin. Other remedies, in the presence of imperiling hemorrhage are a waste of time. Even adrenalin tape is more potent in its local effect if dusted with coagulose powder previous to being packed into a bleeding wound or oozing cavity.

In known hemophiliacs coagulose should be administered hypodermically for some days previous to operation, and pituitrin should be given intramuscularly if the patient shows the slightest tendency to bleed or if cardivoascular tone is imperiled by anesthetic toxemia due to overdosage or persistent cyanosis or shock from any cause whatever.

Remarkable as it may seem the present routine treatment of pyorrhea alveolaris with emetin hydrochlorid is playing an important role in properly preparing unfit subjects for withstanding operative ordeals under anesthesia and analgesia. While the physiological action of emetin hydrochlorid on the circu-

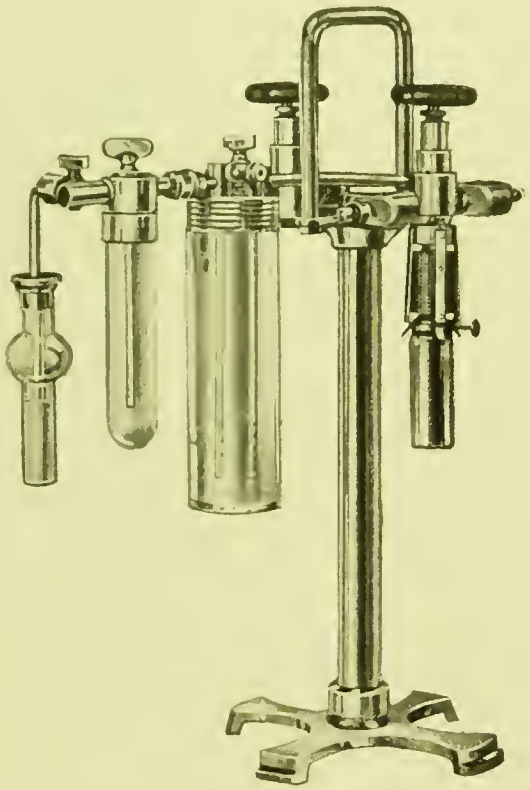

Figure 11. The Gwathmey apparatus showing the sight-feed method of controlling the percentage mixtures of the gases.

latory system has not been finally determined, its use to clear-up gum conditions incidentally provides the operator with a potent means for stabilizing circulatory disturbances due to toxemic pathology. Its value in this connection, however, is not sufficiently realized or appreciated.

The use and value of blood pressure readings with regard to diagnosing certain preoperative conditions or anticipating the onset

of complicated shock, need not detain us as the subject has already been dealt with in a masterly manner. (See E. I. McKesson: Blood Pressure under Anesthesia, herewith printed in the Year-Book.)

As a matter of selfprotection no member of the allied professions should ever administer anesthesia or analgesia to minors without the consent of their parents or guardians, and never under any circumstances whatever to a woman, young or old, married or single, except in the continued presence of the nurse or lady assistant. Operators have forfeited accounts, lost good patients, been mulcted of heavy damages and even imprisoned for imaginary offenses which assumed absolute realities in the erotic hallucinations of women patients under anesthesia and analgesia.

QUALIFICATIONS OF THE SUCCESSFUL ADMINISTRATOR; RELATIONS WITH PATIENTS; KNOWLEDGE OF THE APPARATUS AND ADMINISTRATIVE TECHNIC.

The essential qualifications of the successful administrator of nitrous oxid-oxygen anesthesia and analgesia are *tact and skill.* Where the blunt and illmannered boor will antagonize his clientele, the tactful anesthetist will establish himself in the uttermost confidence of his patients and secure their undivided and enthusiastic co-operation. He must be able to inspire sufficient confidence to obviate all fear of the contemplated narcosis or operation in the minds of his patients. The amount of confidence he inspires will be in direct proportion to his inherent capacity for successful work. The anesthetist without a thoroughly competent knowledge of his apparatus and all the inticate details of administrative technic, has no place in the administration of nitrous oxid-oxygen anesthesia or analgesia. It is no bungler's job, but rather the crowning achievement of a qualified expert.

The expert who extends the beneficence of nitrous oxid anesthesia or analgesia to his patients, whether in dentistry, major or minor surgery or the specialties, can command his own price for his work and feel the assurance of deserving it. Its use is no longer a luxury but an economic necessity as it conserves not only time, but wear and tear on operator and patients alike. The mere fact that nitrous oxid-oxygen is the anesthetic or analgesic of choice in extrahazardous risks, should make it, unless specifically contraindicated, the routine agent for all.

Constant study and prolonged experience alone will fit the tyro as a nitrous oxid-oxygen expert. Even then he will not be successful unless he can command the confidence and co-operation of his patients. Most patients dread anesthesia or analgesia on account of fear borne of ignorance. The expert who informs his patients just what to expect and how to co-operate to avoid complications, will have no difficulty in handling them unless they are hopelessly unmanageable. The various sensations during the induction of analgesia, its continuance or during lapses into anesthesia and vise versa, are not unpleasant, *but they are unusual and unexpected, and unless patients are familiarized with their character and sequence, they may misinterpret these normal sensations as symptoms of approaching faintness, collapse or dissolution.* Also patients operated on under analgesia should be gradually initiated into its mysteries and possibilities, and should not, under any circumstances, be made the immediate victims of prolonged, gruelling procedures under its influence. Such misguided zeal defeats its own purpose. A brief procedure, skillfully and painlessly performed, without untoward effects, will convince the most skeptical patients of the value and utility of the method and they will hasten to requisition it at every possible future opportunity.

Aside from personal skill, intuition and judgment in its administration, the successful use of nitrous oxid-oxygen anesthesia or analgesia depends, in great measure, on a thorough working-knowledge of the latest models of apparatus and their accessory devices, and the keeping of them in perfect working condition. In gaining experience in clinics it is always advisable to use the latest obtainable models of apparatus, even if you have to supply them yourself. Working with a poor apparatus is demoralizing both to skill and results. It is a good idea to become thoroughly familiar with the mechanism and in the use of different makes of apparatus, so that under all circumstances you will be prepared to render

expert service in private practice or public demonstrations.

THE NASAL ADMINISTRATION OF NITROUS OXID-OXYGEN ANESTHESIA AND ANALGESIA

The nasal administration of nitrous oxid-oxygen is of comparatively recent development. In 1892, Clover renewed interest in prolonged nitrous oxid anesthesia. He continued the narcosis induced in the usual manner by passing the gas through a metal tube into the mouth. This method with the mouth hook is in routine use today and has been improved by various types of oral inhalers. In 1898, Coleman revived the use of the nasal inhaler, previously adapted to etherization, and Patterson, in 1899, modified Coleman's inhaler and adapted it to his own improved apparatus. In 1902, Kilpatrick further improved the nasal inhaler by adding an expiratory valve that could be thrown in and out of action as desired. In the same year Hilliard used endopharyngeal nitrous oxid-oxygen anesthesia by means of soft rubber tubes passed through the nares into the nasopharynx. Teter has perfected the nasal technic by adding a pressure-regulated expiratory valve to both the nasal inhaler and the endopharyngeal tubes.

At the present time the technic of the nasal administration of nitrous oxid alone or in combination with varying admixtures of air or oxygen, has become so perfectly developed that it is available for practically all operative procedures in surgery, dentistry and the specialties.

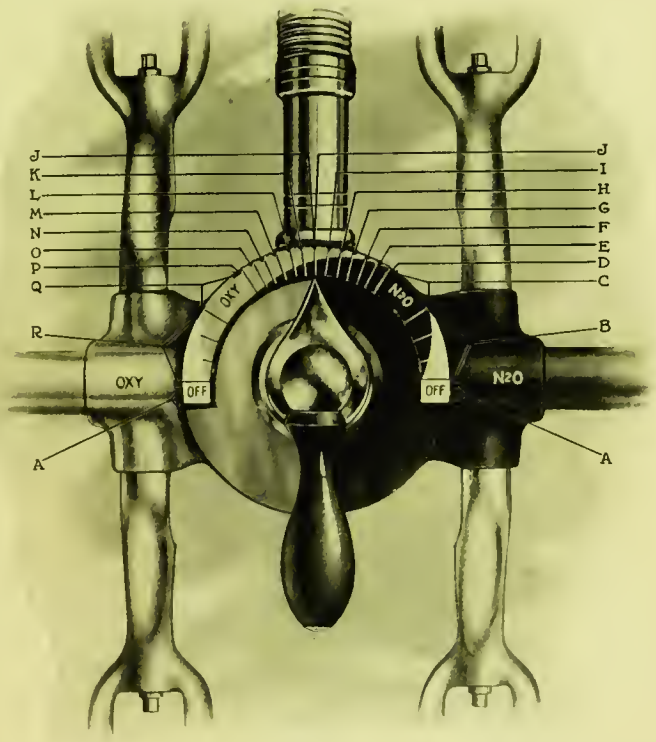

Figure 12. The A. C. Clark valve regulator, indicating the ascending and descending mixtures of nitrous oxid and oxygen as the handle is turned to left or right.

NITROUS OXID-OXYGEN ANALGESIA

Historical Considerations.—In the early days of the discovery of anesthetics practically all operations were performed under analgesia or evanescent anesthesia. Intermittent administration was the routine with nitrous oxid,

ether and chloroform. Crawford Long was the only one of the original discoverers who administered ether continuously, until John Snow in England, at the instigation of Liston, placed the continuous administration of ether and chloroform on a scientific basis of laboratory research and clinical practice. Sir James Y. Simpson used chloroform analgesia as well as anesthesia in obstetrics and shortly after Austin C. Hewitt, of Chicago, imported some chloroform from London, at a cost almost ruinous to his slender means, and after experiments on animals and himself, developed a method of dental chloroform analgesia, under which for some 50 years he successfully performed the various operative procedures now done under nitrous oxid-oxygen analgesia.

Klikowitch was perhaps the first investigator who differentiated the condition now known as *analgesia* from nitrous oxid anesthesia, when in Petrograd in the early eighties he used nitrous oxid analgesia for the alleviation of pain in labor. Nitrous oxid-oxygen analgesia is of very recent development and many authorities and personalities in anesthesia, surgery, the specialties and dentistry have contributed researches and technical improvements.

Definition.—The definition of analgesia as given by Guedel is excellent and comprehensive:

"Analgesia, as ordinarily defined, is that state in which the sensation of pain is lost without the loss of the sense of touch or general consciousness. . . . The pain sense is not wholly abolished; neither does the tactile sense remain unimpaired. The threshold of stimulus to the pain sense is ordinarily decidedly elevated in analgesia and consequently a greater stimulus (traumatism) is required to elicit painful sensation than is necessary to produce the same pain without analgesia. . . . It is true that with the ordinary anesthetic agents the sense of appreciation of pain is abolished before consciousness is lost, but so shortly before that the two phenomena almost meet; and it is not an easy matter to carry the patient along within that narrow latitude which separates narcosis and the

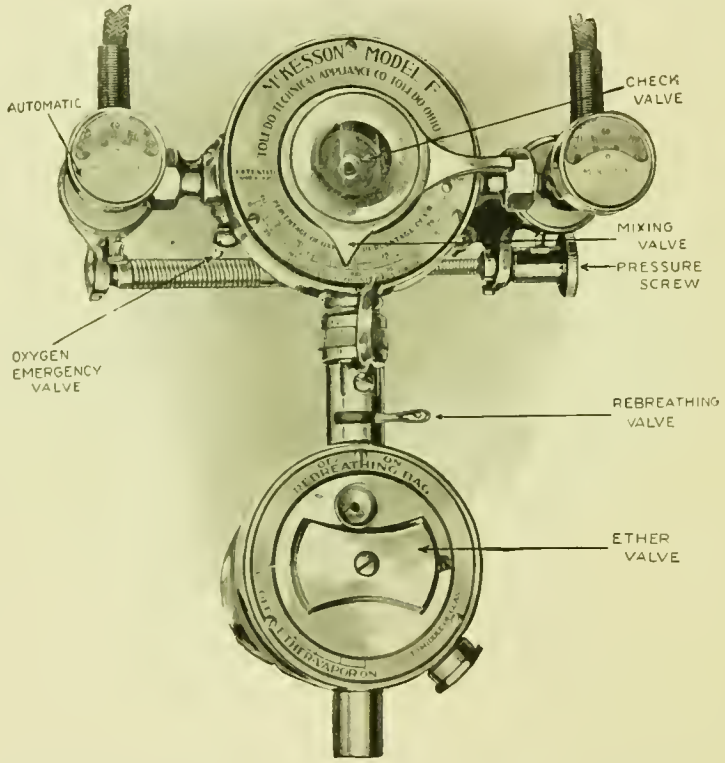

Figure 13. The McKesson apparatus, showing automats; mixing valve; pressure screw; rebreathing valve and ether attachment for supplementary narcosis.

abolition of the pain sense. To do this is to secure ideal analgesia with the patient free from the pain of the operation, yet in the possession of his mental faculties, although their activity may be considerably depressed. In this state of analgesia the patient will respond to suggestion but slowly and with apparent effort. He is in a condition of general intoxication not unlike that produced by alcohol.

Sensations Under Analgesia.—There are slight differences in the sensations resulting from analgesia in different individuals, but a careful analysis shows that the more common sensations are as follows:

Shortly after beginning the induction of analgesia the anesthetic can be *tasted*, and a little late it can be *smelled;* after which the patient begins to *feel* its effects. Barber, of Chicago, has encountered patients so susceptible to nitrous oxid that analgesia supervened synchronously with the tasting of the gas.

The first unusual sensation is one of warmth throughout the body, followed by a sensation of speed, undoubtedly due to accelleration of the pulse and a slight rise in blood pressure. The voice takes on a guttural sound and the patient experiences a thick, large feeling, the result of slight engorgement of the superficial blood vessels, followed by an exaggeration of all sounds, an increase in the apparent distance of objects, a spinning or swinging sensation and tingling in the skin, usually associated with the appearance of perspiration in the palms of the hands or on the forehead, especially in stout subjects. Immediately after a general numbness, apathy, slight incoordination and tired feeling develop, while the sensations of sound and touch become somewhat dulled and vision blurred. Remarkable as it may seem a clear line of demarcation usually separates the realization of outside impressions, such as surroundings and pain, from reasoning ability, throughout analgesia. Mental aberration of any extent only occurs if the stage of excitement is allowed to develop, although momentary aberration may be noticeable when the analgesia is discontinued and all the mental processes and special senses re-establish functional activity with *confusing rapidity*.

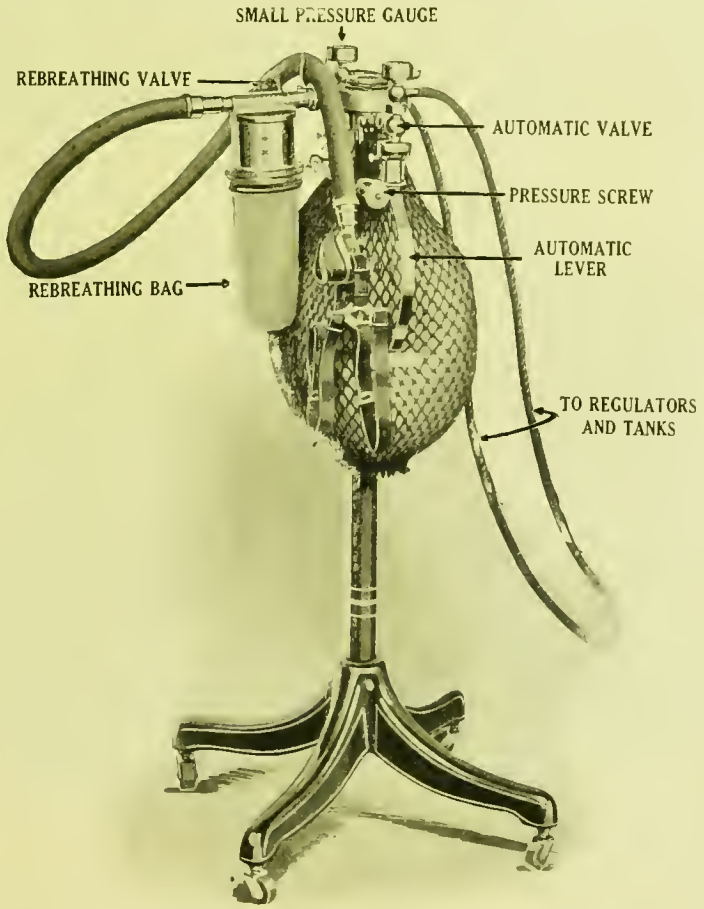

Figure 14. The McKesson apparatus showing the fractional rebreathing bag and the automatic levers controlling the pressure in the bags.

The state of analgesia is made possible by the fact that in the development of general anesthesia the *first special sense to surrender is the sense of pain, leaving the other special senses less influenced.*

Guides to Analgesia.—Impairment of the sense of direction is a reliable guide to the the onset of analgesia. If a patient cannot readily locate his mouth and his efforts to do so are jerky and undecided, the sense of pain will usually be sufficiently obtunded for light operating. The eye, however, is a more accurate indicator of the depth of analgesia. Normally under analgesia the eye should wink lazily and vision should be slightly blurred. As analgesia deepens the eye-ball will rotate from side to side. Pain will be noted in a slight twinge of the eye more quickly than by any other sign. On the contrary, if the winking becomes too sluggish or the lids remain closed the patient is going to sleep. He must then be gently aroused or the analgesia lightened. Occasionally the eyes will become set and the patient stare fixedly ahead. This is a premonitory sign of the onset of a stage of excitement, and must be immediately remedied by decreasing the flow of the anesthetic. Closing of the mouth is another indication that the patient is approaching anesthesia, and to take advantage of this guide, as well as to enable the patient to swallow during operation, it is advisable not to use a mouth prop during analgesia. No stage of analgesia is satisfactory unless the patient is relaxed and indifferent to everything except the explicit directions of the operator for his co-operation. The fearful or neurotic who will not relax under analgesia should be handled under anesthesia.

Hilarity on the one hand and excitement or lapsing consciousness on the other indicates the extremes of analgesia. The former is due to too much oxygen, the latter to pushing the anesthetic; although as Guedel points out, continuous analgesia is prone to lapse into anesthesia due to a peculiar cummulative effect in the system. (See A. E. Guedel: Nitrous Oxid in Obstetrics: herewith printed in the Year-Book). Some patients are so susceptible to the exhilirating effects of oxygen that they can only be properly handled with minimal amounts of oxygen, or with nitrous oxid and air, or even with nitrous oxid alone

Figure 15. The Heidbrink nasal inhaler in use with the rebreathing bag directly attached, instead of to the apparatus.

Others are so susceptible to the potency of nitrous oxid that they require the admixture of apparently excessive percentages of oxygen.

Any sign of suffering on the part of the patient is an indication that analgesia is not complete. Some few patients will demand anesthesia because they refuse to remain conscious to even the slight discomfitures of the sensations of sight, sound and touch. Others, owing to the disappearance of the sensations peculiar to analgesia, which usually subside after analgesia has continued from 10 to 15 minutes, will become disconcerted and imagine that the analgesic condition is evanescing, unless told that the occurrence is usual and that insensibility to pain will persist. Such complete saturation with the anesthetic frequently calls for an elimination of the gases until symptoms of pain perception reappear.

Utility.—Barber maintains that provided the administration becomes proficient, he can get satisfactory results in at least 95 per cent. of his oral procedures under analgesia, while the other small percentage will be readily handled under anesthesia and will be made up of those addicted to drug habits, alcoholics, heavy users of tobacco, patients in whom fear cannot be overcome and those in whom some pathological condition renders the administrative technic difficult or extremely hazardous.

Regarding its use in dentistry, Barber says:

"There are very few procedures in dental practice for which analgesia should not be used. We use it for preparing cavities in sensitive teeth and grinding down teeth for crown and bridge-work. We use it in preparing devitalized teeth for crowns and bridges because of the fact that many times the mental strain of the patient, caused by the noise of grinding, is so great that he suffers postoperative shock to some extent. It is also used in ligating the rubber dam, in setting crowns and bridges, in inserting fillings and in various minor dental operations such as drying out the cavities in the teeth with hot water or cold air, or taking the wax impression for gold inlays and placing temporary fillings. *It is particularly valuable in the treatment of pyorrhea.* This I believe to be still more painful than cavity preparation, particularly when the instrumentation system is used. All this work can be successfully accomplished in most cases without discomfort to the patient, where the ordinary rules for administering analgesia are followed. Occasionally in the deeper pockets it may be necessary to drop into anesthesia at the finish, but we usually do the lighter part of the operation first and administer complete anesthesia near the end of the sitting. The change from prolonged analgesia to anesthesia can be easily made without the knowledge of the patient and the operation completed without any difficulty whatever and with gratifying results."

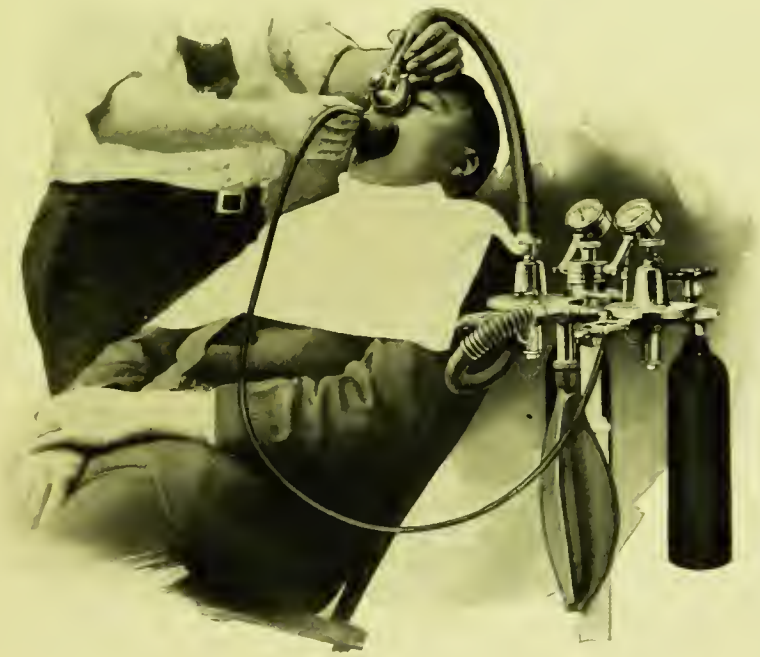

Figure 16. The Heidbrink nasal inhaler in use in conjunction with the mouth cover to deepen anesthesia.

In this connection a note of warning must be sounded against the danger of devitalizing pulps under analgesia by overheated burs. Sharp burs are essential to good dentistry both in eliminating friction and in promoting rapid operating. About two-thirds of the pain in cavity preparation is caused by overheating of the bur, and consequently in fast operating the air syringe should be used to direct a stream of cold air against the bur, under about 30 pounds of pressure, to obviate overheating and also to dehydrate the cavity. Dehydration itself is an important factor in obtunding sensitive dentine. In using stones to grind live teeth, they should be dipped in water every few revolutions to keep them cool.

While such authorities as Allen, Davis, Lynch, Webster, Heaney, Turner, Bastian and Guedel have worked out the technical application of nitrous oxid analgesia to all phases of normal labor and operative obstetrics, Guedel has gone further and has put the self-administration of nitrous oxid and air or oxygen into use as the method of choice in minor surgery in the office and hospital clinic. Evans, of Buffalo, is capping the climax by the successful introduction of analgesia into *major surgery*. (American Journal of Surgery, Anesthesia Supplement, April, 1916). The author in a rather limited experience has been rather favorably impressed with the possibilities of analgesia for a large number of routine genito-urinary procedures. The utiliy of analgesia in the various specialties remains to be worked out methodically. The spirit of investigation is abroad, however, and interesting developments are in the making.

PREPARATION OF PATIENTS

Aside from attending to the usual toilet necessities before submiting to analgesia, patients should have their clothing so adjusted or removed that there will be no interference whatever with respiration under any circumstances or conditions. The assistant should attend to these preparatory details according to a prearranged, routine schedule and compliance with these requests should be insisted on. Further than this it is advisable to cover all patients with an operating gown or sheet of impervious material to protect them from untoward incidents during the course of analgesia or operation.

Co-operation of the Patient.—Success depends not only on preparing patients for the sensations they will experience under analgesia, but also on initiating them into the details of the method by which they can personally co-operate in favorably influencing the zone of analgesia to be maintained. While analgesia is primarily governed by the mixture of the gases delivered, its administration can only be controlled by the integrity of nasal respiration. Oral breathing dilutes the anesthetic with an increased amount of oxygen and an unnecessary and undesirable volume of inert nitrogen, and wide fluctuations in the zone of analgesia rapidly supervene. Consequently the anesthetist must impress on all patients that nasal breathing is of paramount importance in maintaining the proper level of analgesia; and that its depth may be influenced either by alterations in the volume of breathing or by intermittent oral respirations, as may be required. The majority of patients quickly grasp the knack of this method of co-operation and it is only when they resort to oral breathing through confusion or apathy that the anesthetist must regulate the analgesia, for the time being, mechanically.

Patients are preferably initiated into the mysteries and intricacies of nitrous oxid-oxygen analgesia by the self-administration method, in which they not only control the supply of the gases, but may also experiment with the modifying effects of nasal and oral breathing, until they are sufficiently reassured and experienced to accept the nasal inhaler and head-harness with full confidence and a feeling of *preparedness*.

Posture.—Patients may be placed in any of the usual postures that facilitate the operative procedure and do not embarass respiration or promote the inspiration of debris, blood or secretions. Operating tables should be thickly padded to render their otherwise hard surface endurable. In the dental chair patients must first of all be made comfortable or during operations of any length they will grow restless. The most acceptable posture is that assumed in reading a paper in a Morris-chair, with the head tilted far enough forward to allow secretions to flow out of the mouth,

when it is open. The pads of the head-rest should be placed against the occiputs, not the musculature of the neck. The back, although relaxed, should be well supported in direct line with the neck to provide for an unimpeded airway. The arms should be limp and the hands lie in the lap, unclasped. The trunk should occupy the full depth of the chair seat with the legs comfortably extended and the feet resting on the footboard, so adjusted as to offer no point of purchase should patients lapse into the stage of excitement and become obstreperous. (See Edward S. Barber: The Obstreperous Dental Patient: herewith printed in the Year-Book).

Accessories.—In operating under analgesia *with* the rubber dam in position the use of an unbreakable metal saliva ejector is essential. In operating *without* the rubber dam the use of the saliva ejector is not so necessary or of so much service, since the accumulation of secretions is a positive indication of the presence of a sufficient amount of debris to call for cleansing the oral cavity with sponges, cotton rolls or the water syringe. While the use of the rubber dam ordinarily prevents the accumulation of the debris in the mouth and throat and while it renders the control of analgesia easier and more satisfactory, it is a dangerous obstruction fraught with peril to the tyro who is mastering the technic of nitrous oxid-oxygen analgesia. Once the details of its administrative technic have been mastered, then the rubber dam becomes a valuable accessory in facilitating the operative procedure and in controlling the analgesia. A mouth prop should not be used during analgesia as it interferes with the co-operation of patients and prevents the involuntary closing of the mouth, which is a premonitory sign that patients are lapsing into anesthesia.

THE TECHNIC OF THE NASAL ADMINISTRATION NITROUS OXID-OXYGEN FOR ANALGESIA

Adapting the Nasal Inhaler.—While patients are being initiated into the advantages of analgesia it is advisable to let them control the procedure by the self-administration method. Their confidence and co-operation once secured the nasal inhaler and head-harness should be substituted. It is essential to so adjust the head-harness that it will hold the nasal inhaler firmly in place and yet will permit the patients sufficient leeway for necessary movements without disarranging the inhaler. The nasal inhaler itself must be so adapted to the face that it will be air-tight, as any leakeage of air under the rubber cushion will jeopardize the smooth and accurate control of analgesia In some hypersensitive individuals it may be necessary to occlude the ears to spare them the distracting effect of extraneous noises, but in the majority of cases the dullness of the sense of hearing and the response to commands serve as very useful guides to the progress and depth of analgesia.

In adapting the nasal inhaler the valves should be so set as to permit free inspiration and expiration of air until the administration of the gases is begun. Any sense of suffocation at this time is undesirable and disconcerting. The tube from the apparatus, passing up between or behind the pads of the head-rest, must be so adjusted as not to foul and to allow patients to be raised sufficiently to expectorate into the hand cuspidor should this become necessary during analgesia or the operative procedure.

Technic of Administration.—The pressure guages on the large tanks should be set for 30 pounds, which is usually sufficient pressure for any emergency. The reducing valves of the apparatus reduce this to 1 1-4 pounds or less. The flow of gases should be just sufficient to keep the bags about two-thirds full without the aid of any additional pressure device. The flow of gases is increased or decreased to meet the tidal volume requirements of different individuals. The mixture of the gases is regulated according to whether slow or rapid induction is desired and whether or not rebreathing is utilized, and still further according to the desired depth of analgesia and the individual reaction to the percentage demand for oxygen.

In its last analysis the technic of nitrous oxid analgesia consists in diluting the gas with enough air or oxygen to prevent the loss of consciousness, and yet securing sufficient nitrous oxid saturation for the relief of pain.

In inducing analgesia *without rebreathing* both the inspiratory and exhaling valves should be half-open. A percentage mixture of 50-50

is used and the flow of gases is just sufficient to supply the respiratory demand and yet keep the bags fairly well filled. Analgesia should supervene in from 10 to 30 inhalations. If analgesia is delayed the proportion of oxygen is gradually cut down to 20 or even 10 per cent, until the point of saturation, without the slightest cyanosis or respiratory stimulation has been reached. This mixture, then will usually suffice for the remainder of the analgesia, and its control may then be regulated either by manipulating the exhaling valve or by having the patient co-operate by alterations in the nasal respiration or by occasional dilutions by oral breathing.

With rebreathing the mixing valve is set at nitrous oxid 93 and oxygen 7 per cent., from the beginning, and usually this mixture is not changed and the analgesia is regulated by the air dilution at the inhaler. The rebreathing bag is set for one-half the volume of tidal respiration.

To quickly secure complete analgesia in from 3 to 7 breaths, the inspiratory valve on the nasal inhaler is kept closed until analgesia supervenes, when it is adjusted to whatever extent accommodates the requirements of the patient and the desired depth of analgesia.

The slow method starts the patient with the expiratory valve one-half to one-fourth open and the induction requires from 1 to 2 minutes. When analgesia of the desired depth supervenes the expiratory valve is opened a trifle wider and the operation is cautionsly begun while the patient continues to breathe through the nose. If the mouth begins to close, the eyelids droop and answers to directions are sluggish, the patient is lapsing into anesthesia and the air valve must be opened wider, whereas if pain is indicated the air valve is closed a trifle more. This practically constitutes the manipulative part in the adjustment of the apparatus, the mixture of the gases and the regulation of the nasal inhaler.

Depth of Analgesia.—The operator or anesthetist who fully appreciates the proportionate sensitiveness of the various tissues and structures of the body invaded during operative procedures will be able to regulate the depth of analgesia so as to make it correspond to the degree of pain it is required to obtund. Four or five breaths of a richer or more diluted mixture of the gases will usually suffice to respectively deepen or lighten analgesia. The trick is in anticipating the requirements and in realizing that it takes on an average about 32 seconds for alterations in the depth of analgesia to occur.

For controlling analgesia in patients who persistently or inadvertently resort to mouth breathing it is necessary to provide slightly more pressure for the flow of gases and to so regulate the expiratory valve that the gases escape only during exhalation; otherwise analgesia will be evanescent and a waste of gases will result.

Postanalgesic Care.—At the close of any operation under analgesia the inhaler is removed and the patient resumes the ordinary breathing of air. Exertion is contraindicated until after the patient has been fully recovered for some time. Attempts at rapid resuscitation with oxygen perflation will usually cause nausea. Should a dull headache follow prolonged nitrous oxid-oxygen analgesia, then the breathing of a small quantity of oxygen at low pressure will be of material benefit in relieving this unpleasant sequel.

Nausea.—Before concluding the consideration of analgesia it is important to discuss in some detail the incidence and control of nausea, which of all untoward occurrences, is the most disastrous to the satisfactory conduct of analgesia.

While it is always advisable to withhold food from patients for at least 3 hours previous to operations under nitrous oxid, this precaution alone will not prevent the occurrence of nausea and retching. Freedom from exertion on the part of patients under analgesia is one of the prime prophylactic measures in preventing this untoward complication. Consequently the proper position of patients in the chair is essential, so that the only changes in position required may be accomplished by raising or lowering the chair itself, or by assisting the patients to lean forward, slightly, when occasion arises for using the hand cuspidor. Accumulations in the mouth are also prone to cause nausea, especially if swallowed. Therefore, it is imperative for the operator or the anesthetist to prevent the accumulation of debris, blood or secretions by use of the saliva ejector, sponging and dis-

creet use of the hand cuspidor and water syringe. In allowing patients to expectorate, they must be cautiously raised forward by the assistant and not permitted to exert themselves as such exertion may bring on a sickening sensation or unbalanced equilibrium followed by violent nausea.

Disconcerting sights and sounds may become factors in the causation of nausea by distracting patients and interfering with their co-operation and the integrity of nasal respiration, resulting in fluctuations in the analgesia.

The administrator may also precipitate nausea by allowing patients to become cyanotic, or to lapse into the stage of excitement or deep anesthesia and then attempt to revive them by perflation with oxygen. Such decided fluctuations in the zones of narcosis not only effect the circulatory balance of the stomach but also that of the vomiting center.

Duration of Analgesia.—It has been rather conclusively proven by the routine results of experts that analgesia, properly administered to properly prepared and intelligently co-operating patients, may be prolonged for several hours without untoward incidents, immediate or remote.

NITROUS OXID-OXYGEN ANESTHESIA.

General Considerations.—Those who are interested in the problems underlying the narcotic action of nitrous oxid are referred to the researches of Lillie. (See Ralph S. Lillie: The Theory of Anesthesia: herewith printed in the Year-Book). There are a few elements in the administration of nitrous oxid-oxygen by the nasal, oral or combined technic, which are of such fundamental importance that uniform success cannot be obtained without their guidance. The condition of the patient as to the state of anesthesia is wholly determined by the ratio of nitrous oxid to oxygen in the mixture administered, while the reaction of the patient to various mixtures guides the anesthetist in securing the zone of anesthesia required for the contemplated operative procedure.

When a patient is in a state of normal anesthesia he exhibits no response to trauma. If such a state is maintained by a given percentage mixture of the gases, then deviations, one way or another of even 1 per cent. of oxygen in the mixture, will produce corresponding signs in the patient, so exacting are the demands of the human body and so delicate its reaction to potent influences. Consequently the requirements of individuals must be met by adjusting the mixture of the gases according to the reactions of the pulse, respiration and reflexes.

Guiding Signs.—For the sake of classification the guiding signs of reactions under nitrous oxid-oxygen anesthesia may be divided into 4 groups: (1) Respiratory changes; (2) eye reflexes; (3) general muscular manifestations, and (4) degree of oxygenation as shown in the color of the lips, nails or skin.

It cannot be too strongly urged that in determining whether to increase or decrease the oxygen percentage in the mixture *all* signs must be considered. To follow color as a guide, practically to the exclusion of other signs, will prove not only misleading and unsafe, but will result in repeated failures, because the anemic or toxic patient, very often, will not exhibit changes in color until all other signs would show him to be profoundly anesthetized, and then as Cotton and Boothby, of Boston, have pointed out, such a patient may develop an ashen-grey color, far different from the common acceptation of what constitutes a cyanotic reaction. On the other hand, a full-blooded or muscular subject will often show some cyanosis before anesthesia is well established. Similarly the causative factor of muscular rigidity must be differentiated.

For ready comparison McKesson has arranged the accompanying chart of the various reactions under light, normal and profound anesthesia.

A preponderance of the available signs establishes the actual zone of anesthesia as reliably as it can possibly be determined. Regardless of all other signs there are two invariable indications for more oxygen—a widely dilated, irregular, fixed pupil, and cessation of respirations. In either case oxygen should be instantaneously forced into the lungs, once, twice or three times, depending upon the reaction or contraction of the pupils and the returning pink color following the first or second inflations. If respirations have

McKESSON—PHENOMENA UNDER ANESTHESIA

LIGHT ANESTHESIA	NORMAL ANESTHESIA	PROFOUND ANESTHESIA
Due to too much oxygen in the mixture.	Due to a properly balanced mixture of N_2O-O.	Due to too much N_2O in the mixture or to obstruction of respiration.
RESPIRATORY REACTIONS		
(a) Superficial slow breathing usually regular. (b) Prolonged inspiration. (c) Phonation due to reflexes or pain. (d) Holding breath, grunting.	(a) Full "machine like" respirations. Regular and faster than normal. (b) Inspiration and expiration nearly equal. (c) No Phonation. (d) Continuous uninterrupted respiration.	(a) Irregular rhythm (sobby) usually slower than normal. Spasmodic. (b) Prolonged expiration. (c) Phonation due to muscular spasm of vocal cords. Often crowing. (d) Cessation of respiration from spasms of muscles of exhalation.
MUSCULAR PHENOMENA		
(a) Movements or rigid muscles. (b) Facial expression of pain or consciousness. (c) Nausea, very rarely. (d) Reflex, or voluntary resistance.	(a) Immobile and relaxed, but having normal muscular tonus. (b) Expression of normal sleep. (c) Quiet. (d) Quiet. Relaxed.	(a) Clonic movements, twitching or jerking in early minutes of induction, often start in upper eyelids. (b) Expression wild looking. (c) Swallowing, retching or vomiting, common. (d) Tetanic, spasm, marked rigidity—opisthotonus in some cases.
EYE REFLEXES		
(a) Pupils large contract to light actively. (b) Conjunctiva sensitive. (c) Eyeballs roll. (d) Eyelids resist opening, wink when touched.	(a) Pupils small or medium fixed. (b) Conjunctiva insensitive to touch. (c) Eyeballs fixed or slowly roll. (d) Lids often slightly open, relaxed, no winking.	(a) Pupils fixed, enlarge progressively and finally become irregular in shape. (b) Conjunctiva insensitive. (c) Eyeballs fixed in some position or jerk. (d) Eyelids stiff. Often wide open.
COLOR CHANGES IN THE SKIN		
(a) Pink or no change normally. (b) In anemics, no color change. (c) In plethorics, slight cyanosis.	(a) Varies from pink to decided cyanotic tint. (b) In anemics, no color change. (c) In plethorics, considerable cyanosis.	(a) Usually cyanotic. (b) In anemics, slight flushing, rarely cyanosis. (c) In plethorics, almost black.
A green color presenting at any stage of anesthesia is indicative of approaching nausea.		
REMEDIAL MEASURES		
Decrease the percentage of oxygen in the mixture.		Decrease N_2O in the mixture or in (d) inflate lungs with pure oxygen 1 to 3 times.

ceased, they will not begin until 10 or 20 seconds after inflation, or until the excess of oxygen contained in the lungs shall have been absorbed. But the effects on the color index, the eye and other reflexes will become apparent in about 7 seconds after the first inflation.

There is a normal zone of anesthesia obtainable in every patient, but it may be difficult to establish in some patients not properly saturated with the anesthetic from the start, or when the proportions of gases in the mixture fluctuate widely, intentionally or unintentionally, during the operation. Concomitant etherization is frequently used to establish a zone of satisfactory, operative anesthesia in difficult subjects.

THE NASAL ADMINISTRATION OF NITROUS OXID-OXYGEN FOR ANESTHESIA

Since the introduction and perfection of the non-asphyxial nasal method of administering nitrous oxid-oxygen for anesthesia, brief or prolonged, the necessity for hurried operating is a thing of the past. The patients are few and far between who cannot be satisfactorily anesthetized by the nasal technic for any of the operative procedures in surgery, dentistry and the specialties to which the method is applicable.

Adapting and Manipulating the Nasal Inhaler.—The utmost care must be exercised in adapting the nasal inhaler and securing it in position so that air cannot enter as a diluent of the gases. In certain operations the head harness does not suffice and the anesthetist or assistant must hold the nasal inhaler securely in place. The nasal administration of nitrous oxid-oxygen anesthesia calls for a variable amount of pressure in the flow of the gases to prevent air breathing through the open mouth and also the intermittent use of the mouth cover for the same purpose. Intraoral operations necessitating tongue retraction require more pressure than those in which the patency of the air-way is not increased. However, when adventitious growths impede the passage the mouth hook must be used, along with the nasal inhaler, to provide a supply of nitrous oxid-oxygen adequate for anesthesia.

The technic of administration is best mastered by allowing analgesia to lapse into anesthesia in the most favorable subjects, and then continuing the operative procedure and manipulation of the apparatus and accessories, while the patient's condition and reactions are critically observed. The specialist who attempts to conduct anesthesia and to operate at one and the same time, has a man's job on his hands. As Barber says:

> "Cavity preparation under anesthesia is a most difficult matter because of the fact that the operator has so many things to watch at one time. He must operate in such a way as not to expose the pulp of the tooth; he must be careful not to cut the cheek or tongue in grinding; he must keep the watery secretions out of the cavity so he can see; he must prevent the accumulation of debris and blood, the swallowing of which would cause strangulation or nausea. He must observe the patient's color, the size of the tongue, and control the depth of anesthesia by the deft manipulation of his apparatus. Then he must be careful not to operate too rapidly or he may overheat the tooth and cause death of pulp tissue."

Preparation and Co-operation of the Patient.—The preparation of patients for anesthesia is exactly similar to that for analgesia However, if anesthesia is to be induced from the outset, patients must be duly warned not to attempt to influence its course by co-operative changes in their breathing. Respiration should be as normal as possible, under the circumstances, otherwise an element of suffocation will be introduced into the induction.

Technic of Administration.—The tank guages and reducing valves of the apparatus are regulated as for analgesia. The variable amount of pressure required to offset mouth breathing is accomplished either by the automatic pressure devices on the various makes of apparatus or by the tension of the expiratory valve on the nasal inhaler, or both.

With the patient comfortably seated in the chair or in proper posture on the table, and with the nasal inhaler firmly secured in position, several breaths of air are allowed, while a slow flow of nitrous oxid is started. The patient should keep the eyes closed to shut out disconcerting sights and the ears may be occluded with advantage to keep out disturbing and exaggerated sounds. After several inhalations the air-valve is closed tight, so that the further induction and maintenance of anesthesia may be definitely controlled by the admixture of oxygen in varying proportions. Oxygen is added as soon as the first labored

respiration is noted, and its percentage is gradually increased up to 10 per cent. With the first sign of the lapse of consciousness the mouth prop is adjusted and the mouth cover placed in position to obviate the slightest admission of air. The expiratory valve is tightened down one-half. The flow of gases is increased sufficiently to keep the bags full against the automatic pressure regulators. Anesthesia will usually be complete in from 1 1-2 to 2 minutes. Failure of anesthesia is usually due to air-leakage or improper manipulation of the apparatus and accessories. A few whiffs of pure nitrous oxid will remedy this condition, pending a readjustment of the mixture and proper adjustment of the inhaler; while a few whiffs of oxygen will control the opposite extreme, cyanosis.

Cyanosis is due either to a disproportionate amount of nitrous oxid or a degree of pressure in the flow of the gases that impedes breathing. In the one instance the percentage of oxygen must be increased, in the other the pressure must be slightly reduced until repiration is free and easy.

Signs of Anesthesia.—These may be best studied in the guides charted by McKesson. Perhaps the best single test for determining the preparedness of the patient for the operative procedure is the loss of the corneal reflex.

When this occurs the expiratory valve is clamped shut and the mouth cover is removed to permit the operator to proceed.

In the last analysis successful nitrous oxid-oxygen anesthesia, by the nasal method, depends on the administration of such a proportionate mixture of the gases as will effect complete anesthesia without untoward complications, at a pressure sufficient to preclude dilution and fluctuation by mouth breathing.

Utility.—The nasal technic is especially serviceable in anesthetizing patients who have a peculiar dread of the suffocating effects of a face-inhaler. Needless to say it is a necessity for all oral operations under nitrous oxid-oxygen. All dental procedures, as well as many operative procedures of the specialties of oto-laryngological, obstetrical, genito-urinary and minor surgery, can be satisfactorily performed under the anesthesia maintained by the nasal method of administration. Teter, of Cleveland, has used the technic in some 5,000 oral operations of every possible description, utilizing either the nasal inhaler or the endopharyngeal tubes with the pressure-regulated expiratory valve. Denman and McKesson use the nasal method for all tonsil and adenoid operations in children and adults, with the patient in the forward inclined, sitting posture.

Anoci-Association.—This technic of combined local and general anesthesia, established by Crile, of Cleveland, has been adapted to the requirements of dental operations by Riethmüller, of Philadelphia, and Barber, of Chicago. Hoag, of San Francisco, and Davis, Lynch and Webster are using it in obstetrics; while Evans is introducing a combination of local anesthesia and nitrous oxid-oxygen *analgesia* in major surgery through his surgical confreres of the Buffalo General Hospital. The nasal method of nitrous oxid-oxygen administration promises to supersede all others, except in operative procedures requiring etherization for muscular relaxation and the more effective obtunding of pathological tissue. Advantage should be taken of anoci-association practices, whenever they can be used to advantage, as they facilitate the maintenance of a smooth and uncomplicated narcosis.

Handling Emergencies.—During analgesia patients can co-operate in getting rid of accumulations in the mouth; but under anesthesia all debris, blood, saliva and mucous must be painstakingly removed by the anesthetist or operator, either by sponging or aspiration, preferably the latter, as swabbing in the oral cavity tends to precipitate undesirable cough and vomiting reflexes, and leaves the tissues decidedly raw and sore postoperatively. The introduction of a sponge in such a manner as to occlude the oral air-way and yet leave the nasopharynx patent, will materially aid in controlling the aspiration or swallowing of accumulations. The forward-inclined, sitting posture is also serviceable in preventing blood, mucous and saliva from running back into the throat. It seems needless to add that hemorrhage must be controlled by every possible means. As the need for haste in operating has been entirely eliminated in the nasal method of nitrous oxid-oxygen anesthesia and analgesia, the operator can take his time in effectively securing and maintaining a comparatively bloodless field

of operation, even in such procedures as pulp extirpations, tonsil enucleations and multiple extractions.

Occasionally patients will *swallow their tongues*. The consequent embarrassment of respiration is really due to an engorgement of the tissues around the base of the tongue, and attempts at forced oxygenation are futile, until the base of the tongue and the glottis have been pulled forward by a properly shaped tongue depressor. If the mouth prop is a size too large or the mouth gag is opened a notch too far, breathing will be mechanically impeded. Individual patients can open their mouths just so far, without respiratory embarrassment, and no farther. The anesthetist and operator must guage their props and gags accordingly

If cyanosis develops, noted in the color changes of the lips, nails and lobes of the ears, the cause must be immediately removed or remedied and a higher percentage of pure oxygen administered for a few breaths, followed by a return to the percentage mixture previously administered, otherwise patients will come out from under the influence of the anesthesia and nausea result from this violent fluctuation or the attempt to rapidly reanesthetize them. In cases presenting nasal obstruction great care must be exercised in providing a sufficient flow of oxygen under enough pressure to maintain thorough oxygenation.

The onset of nausea during anesthesia is usually indicated by a greenish color around the gills. It may be due to fluctuations in the anesthetic, the swallowing of blood, or the rejection of an undigested meal; but from whatever cause it may arise, the inhaler should be removed, the patient allowed to come out as quickly as possible, and then doubled forward so that the stomach may empty itself with the least possible effort, while at the same time there will be no danger of the patient aspirating any of the vomitus. Of course, the patient must be properly supported and the head held over the hand cuspidor. Cold applications to the back of the neck and face, and the inhalation of aromatic spirits of ammonia will occasionally ward off the incidence of nausea, or control its severity when precipitated. Aromatic spirits of ammonia may also be administered internally, as soon as the patient has sufficiently recovered to swallow it, and this may be followed later by milk of magnesia.

Asphyxia calls for the usual methods of respiratory resuscitation.

Collapse, due to circulatory disturbances, is best handled by the horizontal posture, associated with external warmth and the hypodermic injection of pituitrin. When collapse is due to hemorrhage, colloidal (gelatin) saline solution should be administered intravenously, according to the method of Hogan, of San Francisco, fortified by inhalations of amyl nitrite, and by the subcutaneous injection and local application of coagulen.

SCIENCE MUST RECOGNIZE AS ITS GOAL THE TRUTH—TRUTH FOR ITS OWN SAKE ALONE, WITHOUT CARE—WHETHER, IN PRACTICE, THE TRUTH MAY HAVE CONSEQUENCES, GOOD OR ILL, GRATIFYING OR REGRETTABLE. WHOEVER PERMITS HIMSELF THE SLIGHTEST SUPPRESSION, THE SMALLEST ALTERATION OF THE FACTS WHICH ARE THE OBJECT OF HIS RESEARCH, THAT MAN IS NOT WORTHY TO HOLD HIS PLACE IN THE GREAT LABORATORY IN WHICH HONOR IS A FAR MORE INDISPENSABLE TITLE THAN SKILL. IF IN ALL CIVILIZED LANDS COMMON SUBJECTS OF STUDY BE SO CONCEIVED AND SO PROSECUTED, THEN WILL THEY CONSTITUTE A GREAT COMMON FATHERLAND, STAINED BY NO WAR, MENACED BY NO CONQUEROR, AND WHEREIN HUMAN MINDS SHALL FIND THAT REFUGE AND THAT UNION WHICH WERE OFFERED IN OTHER DAYS BY THE CIVITAS DEI.

—*Gaston Paris.*

HANDLING THE OBSTREPEROUS DENTAL PATIENT . ADJUSTING THE CHAIR AND FOOT-REST . USE OF THE SURCINGLE . VARIOUS EFFECTIVE, THOUGH HARMLESS METHODS OF CONTROLLING UNTOWARD MOVEMENTS ON THE PART OF PATIENTS . NECESSITY FOR KNOWING THESE JIU-JITSU TRICKS, AND PRACTICING THEIR APPLICATION

BY EDWARD S. BARBER, D. D. S. *CHICAGO, ILLINOIS*

BEFORE BEGINNING ANESTHESIA it is advisable to so adjust and lock the head rest that no unexpected movement of the patient will be able to alter its position. With this necessary precaution taken, an obstreperous patient pushing backward with his head or shoulders will find the head rest unyielding and he can be securely held in place as easily as a child (Figure 1).

It is also a very good plan in handling these cases to use a special footboard to prevent the patient from securing a foothold in his effort to push backward. The short footboard illustrated (Figure 2), can be easily fastened to the dental chair and in case the patient does become obstreperous his feet will slide off as it allows him no purchase. Another vital reason for using a special footboard of this type is to prevent the patient from doing himself an injury. A case is reported from Chicago in which a woman became excited under an anesthetic given for extraction purposes and somehow got her foot caught in the footboard of the chair and twisted it to such an extent that her ankle was sprained. When the operation was completed she was unable to walk and sued the dentist for damages and recovered something like $150.00. Such mulcting of damages may be prevented by securing and routinely using an appliance to obviate the occurrence of such unnecessary and unfortunate accidents.

Another simple device for preventing trouble is an ordinary web trunk strap or surcingle with an easily adjustable snap such as illustrated (Figure 3). This strap should be 5½ feet long. I would not advocate a leather strap nor one having an ordinary buckle, for a leather strap is readily torn from one end to the other and the snap must be so constructed as to be quickly adjustable under all conditions, which the ordinary buckle is not.

Figure 1. It is imperative to lock the head rest to prevent any alteration of its position by any movement on the part of the patient.

It is not well to let the patient know that he is being strapped into the chair, but this

can be usually accomplished without his knowledge. An ordinary long towel, such as a bath towel, can be prepared with four straps of cotton tape securely tacked on with thread, one at each end and two nearer the middle, and the trunk strap run under these tapes and the ends folded back in the manner illustrated.

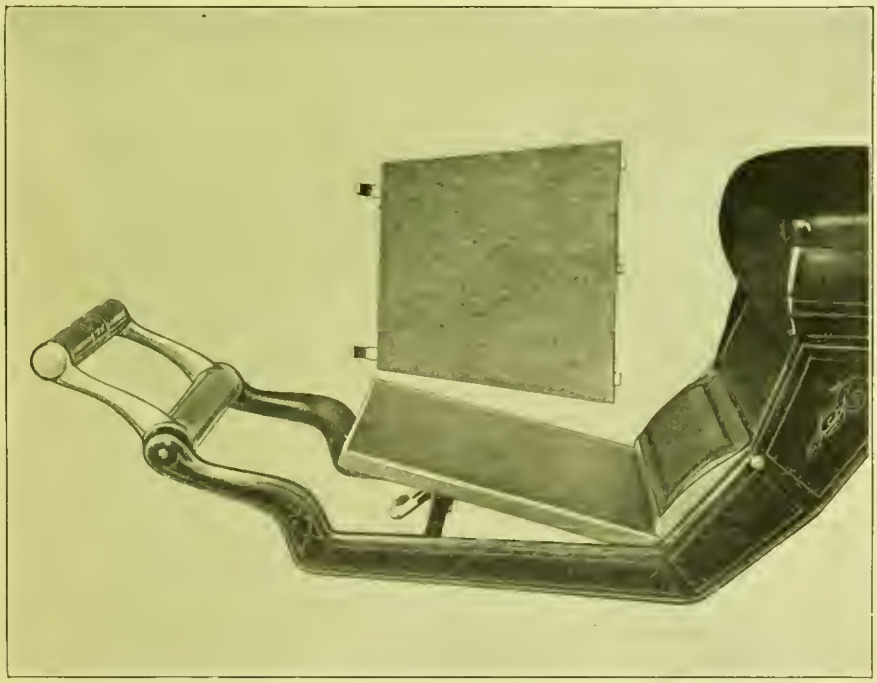

Figure 2. To prevent the patient from bracing his feet against the foot-rest, it should be so adjusted as to present a smooth plane and offer no opportunity for securing a foothold.

Figure 3. Showing method of folding web trunk strap, which is held in place on the underside of a long towel by pieces of tape sewed to the towel.

By folding the towel in one or two long folds the strap is now entirely out of sight and the towel is thrown over the patient's body with the strap underside. It is then tucked in position about the patient's neck at the upper end and with the strap at the lower end just above the elbow. The ends are brought together and fastened behind the chair by means of the slip-catch, with the strap placed between the two levers which raise and lower the back and head rest. In this position the strap is effectively prevented from being raised too far up or dropping too far down. At first the strap should be fastened as loosely as possible so that the patient will feel no pressure and during the progress of the anesthetic's administration it can be drawn tighter in case it is found necessary to restrain him. Care should be used, however, not to have this strap too tight after anesthesia is produced and the patient relaxed, for in that manner respiration might be interfered with. However, there is very little danger from this direction while

the patient is struggling because he will be able to breathe quite readily as long as he is twisting about.

It is possible by the aid of this strap for the young lady assistant to restrain the most obstreperous patient and at the same time hold the inhaler in position after the manner indicated in Figure 4. This leaves the dentist free to use both hands in adjusting the anesthesia and in operating. Usually in the presence of excitement, unless it is due to imperiling cyanosis, oxygen is entirely shut off, while at the same time the pressure on the nitrous oxid flow is increased in order to anesthetize the patient more quickly. Each struggle he makes will become weaker and weaker until at the point of relaxation he will become subdued enough to give no more trouble, and then from 5 to 15 per cent. oxygen may be added and the strap loosened to allow him plenty of room for respiration.

Because of the fact that a great many may not be prepared with the strap to restrain their obstreperous patients and also because many operators are careless and frequently allow the patient to pass from placid analgesia into the stage of excitement, I will show a few illustrations of the commoner methods for holding such patients, which are so simple, safe and sure that anyone can work them out and use them successfully.

Figure 4. Showing the application of the web trunk strap and a simple method by which the assistant can restrain an obstreperous patient.

I have tried the different holds illustrated with some of the best wrestlers in the country and have yet to find a man who could break them. I have also had my young lady assistant hold these patients without difficulty where she

followed my directions absolutely, thereby indicating that the methods do not require strength, but merely skill in their proper use.

In the excitement stage a patient sometimes tries to jump out of the chair in a hurry, and we must drop everything and get hold of him before he leaves the chair because he has very little chance provided the back of the chair does not give way, to get away from it, but once he gets out on the floor it is not only hard to handle him, but there is danger that he may take fright and attempt to jump out of the window.

Man has fought with his hands and legs since the beginning of time and to attempt to hold either during the excitement stage of anesthesia brings on the idea of self-defense. Allow the hands and feet to remain free and let the patient throw them about as much as he desires, but get behind a chair, so he cannot do you injury and then simply hold his head by locking the fingers tightly together and placing the palms of the hands against the chin, and with an elbow lock around the back of the chair it is impossible for him to get away. Of course the bracket-table, cuspidor and other articles must be pushed out of reach so that the patient cannot damage the furniture or injure himself by striking them (Figure 5).

Quite often the patient will grab both hands of the operator and attempt to pull them down. The way of least resistance is to allow the assistant to hold the inhaler on the patient's nose so that he keeps on taking the anesthetic and then allow both hands to fall on the chest, keeping the fingers locked, and allowing the patient to pull on them as much as his heart desires. You will find that he is pulling against himself and the smallest man can easily hold the largest man in this position (Figure 6). This arrangement seems to satisfy the patient and he usually pays no further attention to the anesthetic which will soon overpower him. Whereas, if the dentist tries to pull his hands from the patient's grip he is not only causing himself a great deal of exertion but the in-

Figure 5. Method of holding the head of an obstreperous patient in position against the head rest. At the same time the inhaler and mouth cover can easily be kept in position during the induction period.

Figure 6. In case the obstreperous patient grasps the operator's wrists, it is best to let them fall on his chest where he can be held without effort. The inhaler is held in position by the assistant.

Figure 7. Showing how the operator, unaided, can control an obstreperous patient by throwing the patient's arm behind the chair, using the leg to hold the arm. The operator's arms are firmly held beneath the knobs of the head rest.

Figure 8. Showing the method of restraining the obstreperous patient, when he arches the body and tries to go backward over the head rest. The chair is lowered to a convenient height and the operator places his weight upon the patient's head and is thus able to restrain him easily.

Figure 9. Method of handling the patient who tries to slide out of the chair to the floor. It is necessary to lock the fingers firmly around the chin and to place the crooks of the elbows beneath the knobs of the head rest. In this position the thumbs can support the inhaler in the proper position.

haler is almost sure to be torn off and the anesthetic discontinued.

An additional safeguard in the case where a patient begins using his hands is to draw the arms behind the chair and hold them there until the assistant can strap them down securely. This can often be accomplished by pulling them back with the hands, but in the case of a trained fighter it is not safe to let go his head with either hand, and a simple method is to lock the heel in the hook of either arm and with a sudden, jerking, backward motion throw the arm behind the chair and hold it there with the leg after the manner illustrated in Figure 7.

While the footboard prevents the patient from using much force in pushing backwards over the head rest still they can sometimes get their feet onto the floor and exert a great deal of backward pressure. The chair should be immediately pumped up high enough so that the feet cannot touch the floor, but during the interval the operator should stand on tiptoe and place all his weight on top of the patient's head, and in this manner render him powerless. In this movement the operator's right arm placed on the patient's chest will assist materially in holding him quiet (Figure 8).

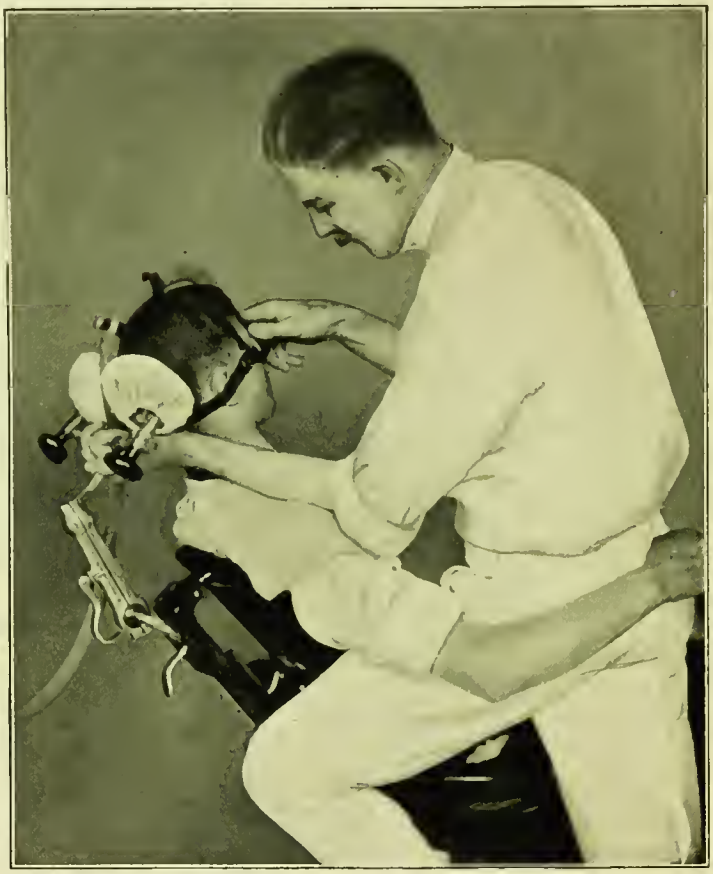

Figure 10. Method of restraining a patient when he suddenly tries to get out of the chair. By grasping the back of the head rest and bringing the elbow down on the shoulder, he can be prevented from going forward. Pressure of the body against the patient's arm will force it behind the chair and his hand will be locked beneath the lifting lever at the back of the operator's knee.

In case the patient tries to slide down out

of the chair this can be prevented by leaning backward and holding him by the chin. Care should be used not to clasp the hands about the neck, however, as this would cause strangulation (Figure 9).

Most dentists prefer to stand in front of their patients during the administering of an anesthetic for the reason that it gives a patient confidence, and it is better to do so for the reason that the color can be closely watched from in front. It is something like matching colors in porcelain work. I find it is almost impossible to notice the beginnings of cyanosis by looking at the patient's face from over the back of the chair, because of the same shadows we have to contend with in matching porcelain facings from the same position.

It is almost impossible to notice the beginnings of cyanosis under any sort of artificial light and sunlight for anesthetic purposes should be used whenever possible.

In order to have the patient under control from this position the chair should be locked so that it cannot turn on its base and the patient's right arm swung out so that when the operator steps backward the arm will be automatically thrown behind the chair by the simple pressure of the body. At any sign of disturbance the operator's left arm is placed on the patient's right shoulder while the operator firmly grasps the head rest beneath the patient's head. By holding the arm stiff the patient can be prevented from going forward (Figure 11).

Figure 11. The right hand of the operator grasps the knob of the head rest, at the same time swinging his body behind the chair, making it impossible for the patient to strike him or move from this position. At the same time the patient's left arm can be easily drawn behind the chair.

Figure 12. Showing method of holding patient's hand until the assistant fastens the trunk strap. The assistant should also keep the inhaler and mouth cover in position at the same time.

I find that professional wrestler's lose all their science under an anesthetic and their whole purpose seems to be to escape. All their force is exerted towards the front and the simple hold illustrated will keep them in position.

In order to make sure that the patient cannot get away, it is a simple matter now for the operator to throw his right arm around the patient's neck, grasping the left knob of the head rest firmly and then pumping the chair up to a convenient height when it is safe to let go with the left arm, and by swinging the body around behind the chair the patient's right arm is locked behind the back and under the lower lever.

It is a simple matter now to draw the patient's left arm behind the chair and hold it in position while the assistant fastens the patient firmly with the strap (Figure 12).

ONE NEED NOT FOLLOW THE ISMS OF THE FADDIST TO BE UP TO DATE., TRUTH IS NOT A MATTER OF TIME OR PLACE, IT IS UNCHANGEABLE. THE ACKNOWLEDGMENT OF THE EXISTENCE OF THE SUPERNATURAL IN THE SOUL OF MAN IS NOT AN EVIDENCE OF REVERSION IN TYPE. IT IS BUT THE RESULT OF THE ACCEPTANCE AND OF THE INTELLIGENT CORRELATION OF A HOST OF FACTS WHICH WE SEE ABOUT US.

ADMITTING THE PRESENCE OF A SOUL, AND AS THE LOGICAL SEQUENCE THE ATTRIBUTES AND ADORNMENTS OF THE SOUL, MAY WE NOT AWAKEN AND DEVELOP THE LOVELIEST OF THESE—CHARITY, SEEING IN MAN, HOWEVER POOR AND ILLITERATE, THE SEAL OF DIVINITY. COURTESY IS HONORED WHEN FOUND IN SUCH COMPANY.

A MAN WHO CAN SEE THE DIVINE HAS AN INCENTIVE WHICH IS IMPOSSIBLE IN THE CASE OF THE MERE MICROSCOPIST. HE CAN UNDERSTAND THAT CHARITY IS ITS OWN REWARD AND AS A CONSEQUENCE HE OFFERS IT WHEN HE CAN.

WE CAN, THEREFORE, IN ADOPTING THE PATIENT'S POINT OF VIEW, ELIMINATE MUCH PAIN AND DISTRESS. THE ACCEPTANCE OF SUCH A COURSE INVOLVES NO EXPENSE. A MOMENT OF THOUGHTFULNESS IS ALL THAT IS REQUIRED. A WORD, A SMILE OR A SYMPATHETIC GLANCE WILL DO MUCH TO LIGHTEN ANXIETY AND PAIN. MORNING OPERATIONS WHEN POSSIBLE; AVOIDANCE OF POSTPONEMENTS; A MORPHIN PRECEDENCE; UNFAILING COURTESY AND CONSIDERATION—ALL THESE MAY SEEM TRIFLES, BUT IN REALITY THEY ARE MARKS OF HUMAN KINDNESS.

IN SUCH MEASURE AS A MAN SPENDS HIS EFFORTS IN DOING GOOD TO OTHERS, IN JUST SUCH MEASURE WILL HE FIND PEACE AND CONTENTMENT WITHIN HIMSELF.

—Paluel J. Flagg.

THE NASAL ADMINISTRATION OF SOMNOFORM ANESTHESIA AND ANALGESIA . PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS . BLOOD CHANGES . SELECTIVE ACTION ON THE CEREBELLUM . STUDY OF THE PATIENT . POSTURES . DESCRIPTION OF APPARATUS AND TECHNIC OF ADMINISTRATION . CARE DURING RECOVERY . HANDLING EMERGENCIES . SHOCK AND COLLAPSE . CARE OF APPARATUS AFTER USE

BY WILLIAM HARPER DeFORD, D. D. S., M. D. *DES MOINES, IOWA*

THE USE OF HIGHLY volatile and rapidly eliminated anesthetics has immeasurably broadened the scope of the expert anesthetist's work in rendering the routine operative procedures of dentistry minor surgery and the specialties *painless.* Also the same agents and methods of administration serve equally well for brief periods of surgical narcosis without the dangers incident to ether or chloroform and the occurrence of their postanesthetic complications.

While ethyl chlorid alone serves admirably as a preliminary to etherization, or when used for minor surgical narcoses, it is in combination with other anesthetic agents that the anesthesia it induces approaches perfection. The combination of anesthetics devised and popularized by Dr. George Rolland, Dean of the Bordeaux Dental School, has been variously modified since its inception, and the formula that has finally established itself in routine use is as follows:

Ethyl chlorid,	83%
Methyl chlorid,	16
Ethyl bromid,	1

By its diffusibility the methyl chlorid secures promptness of action, so that the inhaled anesthetic begins to exert its influence in about the time it takes the red blood cells to travel from the lungs to the nerve centers, where the narcosis is induced. The ethyl chlorid maintains anesthesia and the ethyl bromid provides a stage of analgesia, which is sometimes longer than the duration of the anesthesia itself.

With ethyl chlorid alone the period of induction is longer, the masseter muscles controlling the jaw, are rarely fully relaxed and occasionally take part in the tonic or clonic spasm which is common to the muscles of the extremities. Also headaches, nausea and vomiting are such common complications as to prove a serious drawback to its routine use. Likewise the duration of anesthesia is not sufficient for unhurried operating. The addition of methyl chlorid to hasten the induction of anesthesia obviates the usual spasm of the musclature, while the minimal amount of ethyl bromid which volatizes very slowly at temperatures lower than 75 F assures a rather prolonged period of analgesia, during which while the patient will obey the commands of the operator or is dimly conscious of his surroundings and the manipulation he will suffer no pain incident to light operating.

Heretofore, the use of ethyl chlorid alone or in combination, has been restricted to anesia for the extraction of teeth, but the perfecting of both the formula of the mixture and the nasal method of its administration, now enables the progressive dentist to use this method of anesthesia and analgesia to eliminate pain in such procedures as lancing abscesses, opening inflamed teeth, excavating sensitive dentin and removing pulps.

This method of anesthesia is equally valuable in performing such operations of minor surgery and the specialties as the opening of superficial abscesses, tenotomies, extirpation of aural, nasal or uterine polypi, removal of

tonsils and postnasal adenoids, application of the cautery, passive movements of stiff muscles and ankylosed joints, eversion of toe and finger nails, removal of piles, drainage tubes or dressings from sinuses, curettement, dilatation of urethral strictures, reducing dislocations, making bimanual diagnoses of uterine or ovarian tumors, and in other procedures too numerous to mention.

Ethyl chlorid alone or in combination is invaluable as a preliminary to etherization, not only facilitating the induction and obviating the usual period of excitement, but also reducing by half the amount of ether required to establish surgical narcosis. (See R. A. Rice: Perfected Methods of Etherization: herewith printed in the Year-Book). Ethyl chlorid in combination is especially to be recommended in operations on the upper air tract because no asphyxia is developed; the patient has no sensation of suffocation, there is no cyanosis, no sterterous breathing, and if administered with percentage admixtures of atmospheric air or as Rice suggests, oxygen, jactitation or spasm of the extremities and masseters rarely presents.

Before proceeding further with the practical application of combined ethyl chlorid or *somnoform* anesthesia to the operative procedures of dentistry and minor surgery, it seems advisable to investigate its physio-pathological principles and thus establish its technical administration on a scientific basis.

THE PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS OF SOMNOFORM ANESTHESIA

In experimenting with various combinations of the highly volatile anesthetics, Rolland attempted to secure an anesthetic agent that would approximate the physiological action of oxygen in its entrance into and elimination from the human body. In the combination of methyl chlorid, ethyl chlorid and ethyl bromid, Rolland found an anesthetic which entered the circulation with practically the rapidity of oxygen, had an almost instantaneous narcotic effect on the nervous system and tissue cells, and on the cessation of its administration was equally as rapidly eliminated without causing any appreciable untoward complications.

The extreme volatility of methyl chlorid in this mixture almost immediately on administration establishes an anesthetic tension in the alveoli of the lungs, sufficient to cause its rapid absorption into the circulation and to initiate its narcotic effect within 12 seconds. This preliminary effect is rapidly supplemented by the greater potency of the ethyl chlorid and the slowly volatizing element ethyl bromid serves to sustain an analgesic condition, while the anesthesia proper quickly evanesces with the cessation of its administration.

This rapidity of action may be readily explained. The blood is virtually a gaseous solution, the various gaseous constituents representing 45 per cent. of the total mass. Each ventricular systole throws into the circulation from 135 to 180 grams of blood. As all the blood in the body weighs from 5 to 6 kilos, it requires from 25 to 39 cardiac pulsations for the blood to have accomplished its circulation through the body. The normal heart beats about 72 times a minute. Thus it takes the blood about 25 seconds to return to the heart. From this it is apparent that the rapid absorption of this anesthetic mixture can render it effective in from 25 seconds to 1 minute, the time varying according to the character of respiration, the condition of the circulation and the susceptibility of the patient. The duration of anesthesia and the rapidity of elimination are further exemplified in the clinical observation that anesthesia deepens during 15 to 30 seconds after the withdrawal of the anesthetic, after which consciousness returns in about 1 minute. Thus the available period of unconscious anesthesia (other than in continuous administrations) seldom exceeds 2 minutes, although the minimal amount of ethyl bromid in the somnoform mixture, provides an analgesic period of several minutes more.

THE BLOOD CHANGES UNDER SOMNOFORM ANESTHESIA.

At the Swiss Odontological Congress, held at St. Gall, in 1902, Rolland in collaboration with Muratet and Sabrazes, reported their investigations on the action of somnoform on the blood plasma. Microscopical examinations made before and after anesthesia showed no important modifications, even after anesthesia

had been prolonged 18 minutes. The changes observed were within physiological limits. At the Congress of the British Dental Association, held at Shrewsbury in the same year, Rolland and Field Robinson reported on the pulse, blood pressure and respiration under somnoform anesthesia. These two series of investigations are summarized in Table I. (See also Theodore D. Casto: Blood Changes Under Anesthesia: herewith printed in the Year-Book).

TABLE I.

Blood Changes under Somnoform Anesthesia

Time	Hemoglobin	Red Cells	White Cells		Before Per Cent.	After Per Cent.
Before	102.%	4,991,000	6,000	Neutrophiles	67.48	65.92
				Lymphocytes	26.60	31.84
				Mononuclear	1.90	0.63
During				Eosinophiles	1.25	1.60
18	94.	4,501,200	4,960	Martzellen	0.38	
Mins.				Transitional	1.24	

Time Mins.	Pulse Rate	Blood Pressure	Respiration	Stage of Anesthesia
0	72	13½	16	Before Induction
1	84	14	28	Excitement Stage
2	76	14½	20	Rhythmical Breathing
3	68	15½	19	Deep Anesthesia
4	68	14½	20	Coming out
5	68	12½	20	Analgesic Period

THE SELECTIVE ACTION OF SOMNOFORM ON THE NERVOUS SYSTEM.

Somnoform has a selective action on the cerebellum and it is only after this part of the central nervous system has been saturated with the anesthetic that the cerebrum is affected. This was shown in a series of experiments reported by Cavalier and Rolland at the International Congress of Medicine, held at Madrid, in 1903, and amplified by Rolland before the British Dental Association at the Brighton meeting in the same year.

Certain animals were anesthetized with somnoform and kept so for variable periods of time; others were kept under the anesthetic for about an hour. The animals were destroyed at the end of each experiment and sections from the cerebral and cerebellar cortex were made. These sections were treated, some by Nissl's and Ehrlich's method and others by Golgi's.

In 1887, as a law of the *universality of action of anesthetics,* Claude Bernard propounded the idea of the penetration of anesthetics into every cell of the body. Since then many research-workers have persued this subject and the details of their investigations, theories and conclusions have been summarized elsewhere and a tenable theory of anesthesia finally presented. (See Ralph S. Lillie: The Theory of Anesthesia: herewith printed in the Year-Book). It is admitted that all anesthetics act on the protoplasm by temporarily modifying its various modes of activity by physical, mechanical or chemical action. This action is exercised by the anesthetic, as clinically observed, by diminishing the mode of cellular activity designated as irritability, expressed in motility and nutrition; but like chemical substances in general, an anesthetic has a preferential effect on this or that tissue, this or that organ without changing its universality of action.

There is nothing surprising in this electivity of a chemical substance for a definite portion of the nervous system. It has been definitely established that ether, chloroform and alcohol have in their action a preference for the cerebral covering; that cocain in moderate doses acts on the peripheral endings of the sensory nerves; that strychnin has a predilection for

the cellular elements of the spinal cord; that nicotin paralyses the nervous cells of the sympathetic ganglia; that curare acts on the nerve endings in the muscles and finally that certain other poisons affect the nervous system of the heart.

Basing their theories on the anatomical studies of the nervous system as developed by Waldeyer and Ramon y Cajal, Rolland and Cavalier first directed their attention to a study of the encephalon, assuming that somnoform acted on the higher centers of the nervous system according to their rank. Their results led them to an investigation of the modifications produced by somnoform on the neuron.

Historically there has always been a difference of opinion regarding the influence of anesthesia on the neuron. (1) If von Gehuchten is correct the appendices or dendrites of the pyramidal cell represent a normal disposition of the cell, and when at rest these appendices are filliform: that is to say, of equal calibre throughout. According to this theory the appendices would seem to play a considerable part in the relation of the neurons between themselves. Their normal length and their shape would ensure the integrity of their relations and these relations, in part, would be destroyed by retraction of these appendices or the production of varicosity, nodosity or pearl spots on the protoplasmic prolongations, conditions which have been demonstrated experimentally in the morphological study of the neuron by the chromate of silver staining method of Golgi.

This is the opinion of Demoor, who studied on dogs the lesions produced in the neuron and its prolongation by morphin, chloral, chloroform and other narcotics; of Mdlle. Stefanowika, who studied on the same animals the influence of ether and poisoning by illuminating gas; of Havel and Wright, who showed that the moniliform state is more pronounced in animals subjected to the action of chloroform and ether; of Manouelian, a follower of Mathias Duval, who investigated the lesions of the neuron on mice in an exhausted condition.

In certain experimental conditions the dendrites terminate by a small swelling and become pyriform and then constitute what are called the moniliform or pearl-spot conditions. Also the appendices can further completely disappear.

Unfortunately, however, these reported observations and their interpretation, have not always been confirmed. Azouley, Lugaro and Soukanoff have not been able to observe the disappearance of the appendices and the appearance of the moniliform state under the influence of prolonged administrations of ether, chloroform, morphin or alcohol. According to these authors, it is not so much the influence of the anesthesia as the expression of cellular activity that produces the varicosity or nodosity of the spines and the retraction of the dendrites. According to Lugaro the appearance of varicosities indicates fatigue and this nodosity during repose might cause repair, which would lead to the reappearance of the appendices and to the disappearance of the varicosities.

According to Renauld, of Lyons, the pearl-spot condition is not pathological but a state of physiological activity of the cell and each of the pearl-spots constitutes what he calls an adhesion.

Among those employing Nissl's method of investigating the modifications of the neuron produced by anesthetics, Binz describes the obscure and disturbed granular transformation in the cerebral cells under the influence of chloroform and morphin. Nissl with trianol and morphin has observed structural modifications ending in the destruction of the chromophilous substance of the pyramidal cells. Also the achromatic substance may disappear, the appendices become but faintly visible, the nucleus become small and the nucleolus atrophied. Wright, in investigating the action of chloroform and ether on the neuron of dogs and rabbits in prolonged anesthesia, affirms the rarefaction of the corpuscles of Nissl.

Without entering into the question of nervous ameboism and the independence of neurons, Rolland and Cavalier, in their observations, tried to establish the modifications that the neuron undergoes under the influence of somnoform. They used either the rapid staining method of Golgi with chromate of silver, or the intravascular, vital staining method of Ehrlich with methylene blue, or a combination of these methods as perfected by Cavalier.

Experiments were conducted on non-anesthetized animals, during anesthesia of 5, 10, 15 and 20 minutes duration; at the end of prolonged anesthesia of 1 hour, and on animals anesthetized during an hour after recovery. The accompanying illustrations give a vivid depiction of the results obtained, (Figures 1-12).

of the prolongations farthest from the cell body Repair of the neuron, following deep and prolonged anesthesia, is in the reverse order. It is comparatively rapid, as, in less than an hour, Purkinje and pyramidal cells become nearly normal, the repair beginning in the pyramidal cell and extending to the free extremity of the appendices and taking place more rap-

Figure 1. Pyramidal cell, normal

Figure 2. Pyramidal cell, short anesthesia

Figure 3. Pyramidal cell, deep anesthesia

The salient points in the researches of Rolland and Cavalier may be summarized as follows:

(1) The shape, volume and structure of the pyramidal and Purkinje cells are modified under the influence of any anesthetic, as well as under the influence of somnoform. It seems certain that the fusiform, moniliform, varicose and irregular knotty conditions represent in the prolongations a functional, if not a pathological modification of the normal state. Taking the fusiform state as the first degree, extreme modification is represented by a condition of irregularly situated nodosities joined together by fine filaments.

(2) In their order of appearance these different conditions seem to begin at the portion

idly in the pyramidal than in the Purkinje cell.

(3) The pearl-spot condition seems to be a normal state. It is essentially differentiated from other conditions by the regularity of form and aspect.

(4) While the filliform and pyriform appendices persist even during deep and prolonged anesthesia they are less numerous. Their rarefaction takes place more especially on a level with the varicosities of the prolongations.

(5) The structure of the cell body is modified by the loss of chromophilous substance, beginning at the periphery and attended by rarefaction of the nucleus and nucleoli during deep and prolonged anesthesia.

(6) In conclusion it should be emphasized

that the Purkinje cell is acted upon at the very beginning of anesthesia, while the pyramidal cell still remains intact. In this action of somnoform there is indicated an elective affinity of the anesthetic for this cellular element of the cerebellum. It is only after deep and prolonged anesthesia that the pyramidal cell is in turn affected.

Whatever may be the outcome of von Gehuchten's theory of the dissociation of sensibility, it is apparent that somnoform acts on the cells of Purkinje, by this means suppressing sensibility to pain and to heat and cold, during its passage through the cerebellum; and when saturation or excess of the anesthetic occurs, somnoform reacts on the pyramidal cell, suppressing the sense of touch and bringing about loss of consciousness.

The truth of this experimental conclusion is strikingly exemplified in the clinical technic of *analgesia* with somnoform, in which sensibility to pain and temperature is entirely suppressed, while sensibility to touch and consciousness remain unimpaired, or only slightly affected.

We now turn to the more practical phases of the administrative technic of somnoform anesthesia and analgesia.

THE STUDY OF THE PATIENT

The dentist, anesthetist or surgeon who is to administer any general anesthtic, no matter for how trivial an operation, may with advantage cultivate the habit of observing the patient's physical condition without the patient's knowledge. He may detect at a glance whether the patient is young or old, thin or corpulent, feeble or robust, nervous and excitable, or calm and without dread, temperate or alcoholic, showing shortness of breath or normal respiration. Any serious impairment of the heart or kidneys is also usually apparent.

It is always profitable to note the degree of nervous tension and its form of expression, since this may influence the patient's conduct during the induction and conduct of anesthesia or analgesia. This is particularly true when tension or fear lead to muscular rigidity, gripping the arms of the chair, locking the jaws,

Figure 4. Pyramidal cell-body, normal

Figure .5 Pyramidal cell-body, short anesthesia

Figure 6. Pyramidal cell body, deep anesthesia

opposing the anesthetic or the actions of the administrator. In this connection the allied professions are gradually coming to the realization that neurasthenic and hysterical conditions are symptoms of graver, underlying pathology, probably associated with endocardial or cerebral infections. Consequently in the presence of these complications the anesthetist should be cautious in handling such risks, as they are extrahazardous and may be very susceptible to the toxic effect of any anesthetic.

Signs of intoxication in even mild degree should be carefully looked for, since fear may lead patients to take *a bracer* before entering the office or hospital, and this source of stimulation may lead to excitement or even pugnacity during the induction. Exhaustion from loss of sleep due to pain as well as from prolonged septic infections, require especial attention on account of the feebleness of what Crile terms the *kinetic drive* under these circumstances.

Extremes of age afford no especial contraindications to the use of ethyl chlorid alone or in combination. Flora Murray has pointed out repeatedly that ethyl chlorid is the anesthetic of choice in children and the absence of cyanosis or any tendency to increase blood pressure abnormally, makes somnoform equally as adaptable to the aged with atherometous arteries. The fat or full-blooded patient needs more air in the early stages of induction than a thin, anemic person, although the latter is more apt to suffer from the toxic effects of a prolonged administration. Hypertension and a rapid pulse require cautious induction, while patients with hypotension or even valvular lesions accept anesthesia with remarkable ease and comparative safety. Blood-pressure readings should be made in all, or at least in doubtful cases, as a precautionary measure. (See E. I. McKesson: Blood Pressure Under Anesthia: herewith printed in the Year-Book).

Timid and frightened patients who exhibit their nervous tension must be humored to the extent of beginning the administration of the anesthetic slowly, and in preventing, by a sufficient admixture of air or oxygen, any smothering sensation, or any sudden increase in the heart's action by too strong a vapor. Some patients who fear operation may attempt to conceal their fright under a placid exterior, but their real dread is usually revealed by some disturbance of visceral or vasomotor innervation, such as tachycardia, pseudo angina, polyuria, shallow or sighing respiration, pallor and dryness of the mouth. Scholz, in studying the condition of fearful patients coming to operation, concludes that abnormal fear alone will precipitate acapnia. Such subjects are also prone to exhibit reflex syncope during the induction of anesthesia on account of the irritation of the anesthetic vapor of the nasal terminals of the trigeminus and coincidentally the terminals of the vagus in the heart and in the respiratory center of the medulla. Rosenberg has found that cocain abolishes this reflex andGwathmey overcomes it by the use of oil of orange. According to Scholz, fearful patients suffer a constant decline in blood-pressure during the induction of anesthesia, the average decrease being 45 mm. of Hg. in 15 minutes, or until the stage of surgical anesthesia has been reached. Even then further decreases may be noted, due to operative manipulation or trauma. The untoward effects of excessive fear, according to Cannon and Crile, are probably due to adrenalin exhaustion and consequent imperiling degress of muscular relaxation, in association with undiagnosed endocardial complications.

It seems superfluous to mention that all tight clothing should be loosened before attempting the induction of anesthesia. Corsets must be removed and the nurse-attendant should not only see to this detail of preliminary preparation, but should also warn the patient that toilet facilities are to be utilized before taking the chair.

The expert anesthetist will usually be able to persuade the patient to yield without opposition to the induction of anesthesia or analgesia. The amount of self-control exerted by the patient will be largely determined by the amount of confidence the operator is able to inspire. Nothing will so quickly place the patient at ease as the realization that the operator knows exactly what he is to do and how to do it. Pleasant, diverting conversation or music may play an important part in putting the patient in the proper frame of mind for the ordeal of anesthesia. (See W. P Burdick: The Use of Music During Anesthesia

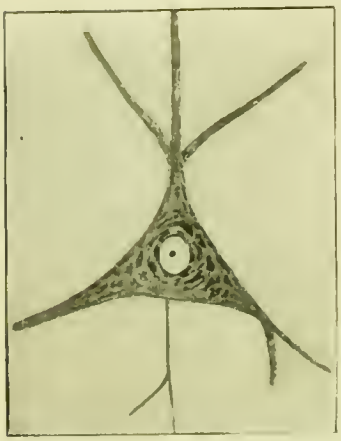

Figure 7. Purkinje's cell, normal

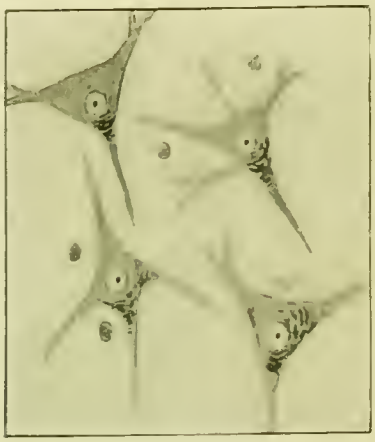

Figure 8. Purkinje's cell, short anesthesia

Figure 9. Purkinje's cell, deep anesthesia

and Analgesia: and J. A. Jarvis: From the Outside Looking In: herewith printed in the Year-Book).

THE POSITION OF THE PATIENT

For many minor surgical operations and practically all dental procedures the semi-reclining upright position answers all purposes. The head-rest should be so fixed as to tip the head slightly backward without stretching the neck or embarrassing respiration. The feet should rest comfortably on the foot-rest, without the legs being crossed or any opportunity given them to secure a purchase should a muscular spasm of the extremities unavoidably occur. The hands should lie limp and unclasped in the lap, so that they may be raised by the patient to indicate pain during analgesia or by the operator to determine the extent of muscular relaxation during the induction of anesthesia. Providing that breathing is not interfered with, the patient should be placed in that position which facilitates access to the field of operation. For all procedures in which somnoform is to be followed by etherization, the usual horizontal, surgical posture is advisable, although with proper precautions and the use of sequestration and the French chair-

Figure 10. Purkinje's cell-body, normal

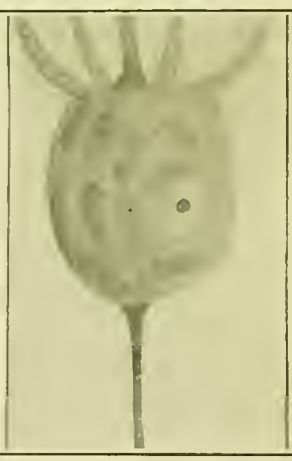

Figure 11. Purkinje's cell-body, short anesthesia

Figure 12. Purkinje's cell-body, deep anesthesia

table, patients may be anesthetized in the horizontal and then operated on in the upright or any other desired position.

The use of the aspirator to prevent the swallowing of blood during dental or oral operations is a refinement of technic, and it is also imperative for the operator to prevent anything else from dropping into the throat during anesthesia. Deaths in the chair have occurred from such accidents and operators, under the circumstances, have been mulcted of heavy damages.

Before inducing analgesia or anesthesia it is well to come to an understanding with patients regarding their respiration. Many persons have a habit of *shallow breathing* which not only poorly oxygenates the circulation but prolongs the induction period of anesthesia on account of carrying so small an amount of the anesthetic vapor to the alveoli of the lungs during each inspiration. While *deep breathing* is neither required nor desirable, moderate respiratory excursions are necessary for the proper induction and maintainance of anesthesia. In using analgesia the operator should explain to the patient the manner in which respiration may be made to assist in deepening or lightening the obtunding effect of the anesthetic. With such a preliminary understanding the patient will co-operate satisfactorily and enable the anesthetist to accomplish anesthesia or analgesia with comparatively no inconvenience.

Postanesthetic nausea is produced almost invariably by administering the anesthetic too soon after a meal, by overdosage or by swallowing of blood. Swallowing blood will cause nausea and vomiting although no anesthetic is administered, while there is no occasion for the expert anesthetist to overdose his patient, particularly when apparatus is at hand by means of which the dosage may be accurately adjusted. Consequently it is important to warn patients about not eating for several hours previous to the administration of the anesthetic; and it is not advisable to attempt anesthesia, analgesia or operation on a patient with a full stomach, except in necessary emergencies. Fasting, the use of the aspirator and the accurate adjustment of dosage will go far toward reducing the incidence of postanesthetic nausea or vomiting. *Acidosis* which may complicate infections and graver pathological conditions, and which is an etiological factor of prime importance in postanesthetic vomiting, must be combated by preliminary carbohydrate feeding, the free use of alkalies and Fischer's solution, and the postoperative exhibition of alkalies, fruit-juices and glucose or sugar to counteract any tendency to edema of the brain, tissues or excretory organs, (Hogan).

DESCRIPTION OF APPARATUS AND THE TECHNIC OF ADMINISTRATION

While ethyl chlorid has been available as a general anesthetic for a number of years, its use for *continuous* analgesia and anesthesia by *nasal* administration has been deferred owing to the lack of suitable apparatus. The De Ford inhaler, devised and developed for the administration of ethyl chlorid or somnoform, now provides the expert anesthetist with a simple, efficient and portable device for administering continuous analgesia or anesthesia.

The essential parts of the device, as illustrated in Figure 13, are: (1) a Capsule Chamber, in which the ampoules containing the anesthetic are fractured; (2) a Gauze Chamber to prevent the entrance of shattered glass into the apparatus; (3) a Rubber Bag to hold the volatized anesthetic vapor; (4) a Regulating Valve, controlling the volume of the anesthetic vapor and the percentage admixture of air; (5) a Nasal Mask with sponge rubber cushion to render it air-tight and adaptable to the contours of varying faces, and an Expiratory Valve, controlled by a milled cap, by the turning of which *rebreathing* may be governed, and finally, (6) a Mouth Cover, used during the induction of analgesia or anesthesia to avoid too great dilution of the anesthetic vapor by oral breathing. Attached to the tube leading from the nasal mask to the rubber bag is a support to render the apparatus stable, when strapped to the head, and allow the operator the freedom of both hands. The mouth cover is adjusted to its proper position by means of an adjusting rod and set screw, and during operation it may be put out of the way by letting it fall back into a slip-catch on the nasal mask.

Assemble the appliance with the exception of the mouth cover. See that the lever of the regulating valve is pushed down as far as it will go, as this prevents the anesthetic vapor from escaping. With the gauze chamber lightly packed, place an ampoule of ethyl chlorid or somnoform in the capsule chamber, replacing the cover, and pressing on it until a slight explosion indicates the fracture of the ampoule. The anesthetic vapor is now confined in the rubber bag and cannot escape until liberated in percentage volume by manipulations of the regulating valve.

previous to inducing anesthesia on account of the occasionally incidence of masseter spasm. The mouth cover is attached to the pin on the nasal mask, and is adjusted to its proper position by the set screw so that it accurately covers the mouth when dropped into position.

When indicated the mouth cover is firmly held in position by pressure of the hand until the analgesic or anesthetic stage has been reached, as it forces the patient to breathe through the nose, and nasal respiration once automatically secured will usually persist throughout the narcosis, even when the mouth

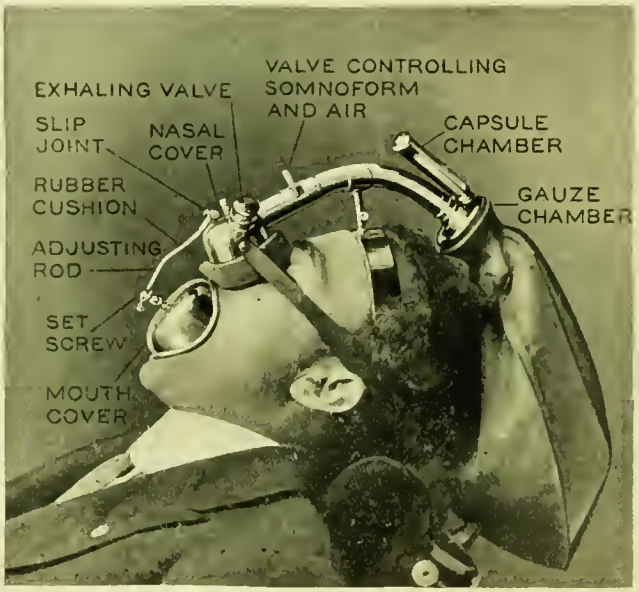

Figure 13. The DeFord nasal inhaler for the administration of somnoform. The various parts are indicated. Mouth cover in place.

For operation on the teeth under analgesia, when the rubber dam is used, the mouth cover is not necessary. For removing tonsils, adenoids and in performing other oral operations under anesthesia, the intermittent use of the mouth cover is important. Also for extraction of teeth the use of the mouth cover is essential during induction of anesthesia or its maintainance should the operation be prolonged.

The apparatus is now adjusted by placing it over the patient's nose and stabilizing it by means of the support and head-strap. It is always advisable to introduce a mouth prop

cover is lifted for the operative procedure. Should oral respiration supervene, however, and imperil the necessary depth of anesthesia, the mouth cover is replaced temporarily until the re-established nasal respiration has again made the anesthesia sufficiently effective.

The valve regulating the relative amounts of air and anesthetic vapor is so arranged that when the lever is pushed as far down toward the forehead as possible, only air is admitted. Raising this lever gradually admits the anesthetic vapor and reduces the admixture of air, so that when the lever is raised as far as possible, the patient inhales the anesthetic vapor only.

THE INDUCTION OF ANALGESIA

It is advisable to complete the painless parts of all operative procedures before beginning the induction of analgesia. When all is in readiness the patient is allowed several breaths of air, then the lever of the regulating valve is slowly raised and the anesthetic vapor gradually admitted in increasing volume with a diminished admixture of air. The lever is raised until the lazy winking of the patient's eyelids indicates the onset of the anesthetic's obtunding effect. Only several more inhalations will then be necessary for an analgesia of brief duration. It is not desirable for the patient to lose consciousness. At this stage operating may be commenced, increasing the pressure and speed of the bur if no pain is felt. When a plane of satisfactory analgesia has been reached the regulating lever should be pushed down to shut off all or nearly all of the anesthetic vapor. The beginner will do well to exclude all the anesthetic vapor at intervals, admitting a fresh supply as required. The expert, with increasing experience, will be able to manipulate the regulating valve to admit just the necessary amount of fresh vapor to make the analgesia smoothly continuous. During continuous analgesia the depth of the obtunding effect is controlled, not only by manipulations of the regulating valve, but also by the tidal volume of the patient's respiration. It is surprising how quickly patients accustom themselves to co-operate with the operator by lightening or deepening the plane of analgesia by increasing or diminishing their respiratory excursions. Also, when operating without the rubber dam, the lips may be closed at intervals to offset the dilutent effect of oral breathing, or the mouth cover may be used. The continuous supply of anesthetic vapor is secured by fracturing fresh ampoules in the capsule chamber.

Figure 14. Mouth cover removed for operating.

THE INDUCTION OF ANESTHESIA

To induce complete surgical anesthesia the anesthetic vapor is gradually admitted by raising the regulating valve. The rapidity with which this can be done will depend entirely on the reflexes of the mucous membrane in accepting the gradually concentrated vapor of the anesthetic. If the patient manifests no uneasiness, the lever may be rapidly advanced

until the patient is breathing the anesthetic vapor only and exhaling it through the expiratory valve. Continuous anesthesia may require various degress of rebreathing, which is accomplished by closing the expiratory valve entirely or partially, and by allowing the rebreathing of the anesthetic vapor to and fro from the bag, or by admitting varying percentages of air as the exigencies of the narcosis may require. The anesthetist who has acquired considerable skill in the use of somnoform for short administrations will find the nasal technic a very satisfactory method of conducting anesthesias lasting upward to 15 or 20 minutes. Continuous anesthesia is preferable to repeated administrations, particularly if hemorrhage can be controlled by packing or the patient kept from swallowing blood by aspirating it mechanically. In the event of repeating the administration at the same sitting, sufficient time should elapse for the patient to fully recover from the effects of the first administration, and this interval should be used to cleanse the mouth and control hemorrhage to avoid spasm of the glottis from the weight of the accumulated blood. In the presence of persistent bleeding or oozing during operations under anesthesia, the aspirator should be moved across the base of the tongue to keep a clear, bloodless operative field.

Figure 15. Rubber dam in position. Nasal inhaler arranged for use of somnoform or nitrous oxid-oxygen as desired.

SIGNS OF ANESTHESIA AND ANALGESIA

During analgesia the patient merely feels drowsy, the eyelids wink lazily and there is some tingling and numbness in the extremities. The patient can talk, is conscious of everything that is being done, but is insensible to the pain of light operating. He is able to assist the operator by moving the tongue or jaws and clearing the mouth. With the onset of anesthesia, however, there is loss of consciousness, muscular relaxation usually supervenes, the eye-balls roll upward, while the pupils noticeably dilate, and breathing becomes rhythmic and automatic as during sleep. As anesthesia deepens the dilatation of the pupils becomes more marked and the eye-balls become fixed, while the corneal reflex is lost and snoring or sterterous respiration occurs. These signs denote the ultimate plane of surgical narcosis that is compatible with safety.

Anesthesia continues to deepen for some 15 seconds after the last inhalation of the anesthetic vapor, and then elimination begins and is usually completed in about 1 minute, although when somnoform is used, the ethyl bromid provides a workable period of analgesia during recovery, which may be utilized to good advantage.

A study of the signs of anesthesia and analgesia as well as close attention to the percentage admixtures of air and anesthetic vapor required to continue analgesia or prolong anesthesia, will gradually develop an "anesthetic sense of intuition," which will enable the operator to adapt the technic of administration not only to the given patient, but also to all the exigencies of the operative procedure in hand.

Analgesia is far more valuable to the dental surgeon than complete surgical anesthesia, because the latter is seldom required, while many times each day, for almost every patient, analgesia can be induced with advantage to both the patient and operator, and much work that would otherwise be painful and protracted, can be accomplished painlessly and in very little time. The public is beginning to understand the beneficence of analgesia and to demand its use whenever possible. Only a broad experience will enable the administrator to determine the necessary degree of analgesia for individual cases. All operations, except the removal of live pulps and extracting teeth, can usually be performed under analgesia without the loss of consciousness; and only in extreme hypersensitiveness of the dentin is it necessary to induce complete anesthesia.

The depth of unconscious anesthesia also varies according to circumstances. Minor procedures of brief duration only require an evanescent degree of anesthesia, while for protracted procedures, continuous surgical anesthesia must be painstakingly maintained.

CARE OF THE PATIENT DURING RECOVERY FROM THE ANESTHETIC

Keeping the patient sitting back in the chair during the time he is coming from under the influence of the anesthetic and talking quietly and soothingly will freqently overcome any vicious or otherwise unpleasant tendencies and will materially assist in preventing nausea. It is not advisable to request a patient, partially recovered from anesthesia, to sit up and spit. There should be at hand a convenient receptacle that can be raised to the lips for this purpose. The mouth can be gently swabbed with gauze sponges thus obviating the necessity for any change in the patient's position, and the mouth may even be rinsed with warm water or antiseptic solutions in the semi-reclining posture by turning the head to the side. The patient should not move or be moved until the immediate effects of the anesthesia have entirely worn off. Vomiting from swallowed bloor or a full stomach always causes a spasmodic thrusting up of the diaphragm against the heart and may cause depression of the circulation and even fainting.

ACCIDENTS

Somnoform anesthesia and analgesia have been singularly free from the accidents of general narcosis. It is very comforting for the administrator to know exactly what to do in case any untoward accident should occur. Experimental research has determined that in laboratory fatalities respiration has ceased several moments before the heart did. Consequently in clinical instances of embarrassed breathing immediate efforts should be made to re-establish respiration. The apparatus should be entirely withdrawn and sudden, sharp pressure exerted on the patient's abdomen. This stirs up the solar plexus and in most instances is sufficient to re-establish breathing. If not, then rhythmical traction of the tongue associated with artificial respiration by lifting the arms and lowering them with compression of the chest, should be instituted and continued about 18 times a minute, until spontaneous respiration returns. Meanwhile nitroglycerin 1-100 gr. may be dissolved under the patient's tongue and amyl nitrite or aromatic spirits of ammonia held to the nose. In cardiac collapse 8 to 10 drops of adrenalin in the conjunctival sac will usually cause a prompt and resuscitative circulatory response. Massaging the precordial area and lowering the patient to the horizontal or slight Trendelenburg posture will materially assist in accomplishing resuscitation.

THE CARE OF THE APPARATUS AFTER USE

As soon as the operation is over and the patient has fully recovered, the gauze in the inhaler should be removed and discarded, and the rubber bag and sponge cushion sterilized by exposure to dry heat and immersion in an antiseptic solution such as lysol, bichlorid of mercury or carbolic acid.

Both sides of the bag should be thoroughly dried and powdered with soapstone, all excess of the powder being then removed. Unless this is done the rubber bag and the sponge cushion will rapidly deteriorate. All metal parts of the apparatus should be sterilized by boiling. This sterilization of the apparatus is an imperative prophylactic measure against the transmission of communicable diseases and should never, under any circumstances, be neglected.

IN DEALING WITH MAJOR OPERATIONS, THE SUCCESSFUL APPLICATION OF LOCAL ANESTHESIA DEMANDS PATIENCE, TIME AND SKILL—A SKILL THAT CAN ONLY BE ACQUIRED AND EXERCISED ON THE HUMAN CADAVER BY THOSE, WHO, BEING ANATOMISTS, CAN ALONE SURVEY THE FIELD OF OPERATION WITH FLUOROSCOPIC EYES. FOR THIS REASON THE PRACTICE OF PERIPHERAL ANESTHESIA, ESPECIALLY IN ITS NEUROREGIONAL ASPECTS, APPEALS MOST POINTEDLY TO THE YOUNG, AMBITIOUS AND WELL-TRAINED SURGEON, WHO, FRESH FROM THE ANATOMIC LABORATORY, FINDS HERE, AS NOWHERE ELSE, AN IMMEDIATE AND PRACTICAL APPLICATION FOR A KNOWLEDGE THAT HE HAS ACQUIRED AT THE COST OF LONG NIGHTS OF VIGIL, LABOR AND THOUGHT.

IN THESE DAYS WHEN EXACT TOPOGRAPHIC AND APPLIED ANATOMY IS RATED SOMEWHAT AT A DISCOUNT, IT IS A SOURCE OF NO SMALL GRATIFICATION FOR THE YOUNG, BUT WELL-TRAINED MAN TO DISCOVER THAT HIS ANATOMIC KNOWLEDGE IS A LIVING, PALPABLE AND PRODUCTIVE ASSET. NOT A THING TO BE LEARNED SOLELY AS A MATTER OF ACADEMIC CULTURE AND SOON TO BE FORGOTTEN, BUT A PRACTICAL TOOL TO BE USED IN UNLOCKING HIS MOST IMMEDIATE TECHNICAL PROBLEMS. IT IS ONLY THROUGH THE AID OF APPLIED ANATOMY THAT REGIONAL ANESTHESIA IS WHAT IT IS TO-DAY. FOR THIS REASON ALONE IT DESERVES THE ENCOURAGEMENT AND FOSTERING CARE OF EVERY SURGEON AND EVERY TEACHER WHO HAS AT HEART THE HIGHER WELFARE OF HIS SCIENCE AND HIS ART.

—*Rudolph Matas.*

FURTHER RESEARCHES IN NOVOCAIN-ADRENALIN ANESTHESIA . ADMIXTURES . ISOTONIA AND PREPARATION OF SOLUTIONS . AMPULES DANGERS OF STALE SOLUTIONS . ADMIXTURES OF ADRENALIN . MÜNSTER RESOLUTIONS . MODIFIED INSTRUMENTARIUM . PREPARATION OF FIELD OF INJECTION . PRESSURE ANESTHESIA . INFILTRATION OR MUCOUS ANESTHESIA . CONDUCTIVE ANESTHESIA . TECHNICAL DIRECTIONS . PREOPERATIVE MEDICATION . THERAPEUTIC MEASURES IN COLLAPSE . POSTOPERATIVE TREATMENT . CONCLUSIONS

BY RICHARD H. RIETHMÜLLER, Ph. D., D. D. S. PHILADELPHIA, PA.

THE ADOPTION OF LOCAL ANESTHESIA by novocain-suprarenin, which for about a decade has been the method of predilection in dental practice on the European continent, in Great Britain, and South America, has been especially dilatory and cautious in the United States. The chief reasons for this seeming conservatism are probably three:

(1) The injudicious employment of cocain and proprietary secret cocain preparations by unethical *painless dentists*, which have inspired the public and the ethical practitioner alike with a fear of the utilization of that treacherous alkaloid.

(2) Frequent failures in local anesthesia due to a lack of appreciation of the physiological and anatomic premises upon which all methods of this specialty are based, and of the imperative necessity of asepsis—of solution, instrumentarium, and field of operation.

(3) A partiality to general anesthesia, apparently justified by the remarkable development of nitrous oxid and oxygen anesthesia and analgesia in this country.

A more discriminating appreciation of the relative merits of nitrous oxid and oxygen general anesthesia and novocain-suprarenin local anesthesia, however, is close at hand, since local anesthesia has, within recent years, found enthusiastic advocates, among both the American dental and medical professions.

REASONS FOR THE INCREASING POPULARITY OF LOCAL ANESTHESIA

The increasing popularity of local anesthesia over general anesthesia is due, besides its incomparably greater safety, absolute certainty of insensibility, and facility of operating, to three factors:

(1) The admixture of suprareneal preparations to the anesthetic solution, as suggested by Prof. Heinrich Braun, of Zwickau, the *father* and pioneer of local anesthesia, by which absorption of the anesthetic into the circulation is retarded, the depth of anesthesia is increased, and anemia in the field of operation is insured.

(2) The substitution of cocain by far less toxic, more stable and uniformly effective, sterilizable, and non-habit-forming synthetic products—among which novocain, or the hydrochlorid of para-amino-benzoyl-diethyl-amino-ethanol is given preference universally.

(3) The perfection of the method of perineural and conductive anesthesia—which again we owe to Braun.

In Braun's[1] and Allen's[2] text-books, designed for general surgery, and in Prof. Dr. Guido Fischer's[3] volume addressed to the dental practitioner, and in an abundance of essays,

chiefly from German sources, which are enumerated in the third German edition of Fischer's text-book, and in Bünte and Moral's monograph,[4] the chemistry, pharmacology, and toxicology of novocain and synthetic suprarenin, alone and in combination, have been thoroughly discussed. The results and arguments of these investigations are fairly familiar to the reader of American medical, surgical and dental journals, in which numerous general articles have appeared on this topic, under the acknowledged—and more frequently under the mute, but manifest—sponsorship of the pioneers mentioned.

NOVACAIN SOLUTIONS AND ADMIXTURES SUGGESTED

Although it has been established by animal experimentation that novocain is seven times less toxic than cocain, and although clinical experience in man has shown this toxicity to be ten times less than that of cocain, attempts have been made to reduce this toxicity even further by the admixture of certain drugs.

PEPTONE ADMIXTURES

I have given due consideration to the suggestion of Fichot and Billard, who, on the basis of interesting studies regarding anaphylaxis, have suggested the employment of mixtures of peptone and novocain.[5] Practical reasons strongly militate against this mixture, since no guarantee is offered as to whether the peptone and novocain solutions are sterile without their having been boiled immediately before injection—to do which is, of course, impossible, as the peptone coagulates on boiling. Moreover, the formation of a wheal and the retardation of absorption of the solution are undesirable.

ADMIXTURE OF HYDROGEN DIOXID

The association of hydrogen dioxid with novocain, as indicated by Marmouget and indorsed by Mahé and Vanel[6] involves the great disadvantage of lack of isotonia. Moreover, we have learned by sad experiences to be extremely cautious in the use of hydrogen dioxid, which may produce grave tissue lesions, especially when injected hypodermically.

ADMIXTURE OF SODIUM BICARBONATE

Gros and Laewen[7] have experimented with novocain- sodium-bicarbonate-sodium-chlorid-adrenalin solutions, claiming for them more rapid and enduring anesthesia, especially in extradural anesthesia and in operations on the lower limbs. Since this method has not found general consideration, and has not been satisfactorily tested out in dental operations, we can limit ourselves to a mere mention thereof. Moreover, these investigators affirm that they could not dispense with the solutions indicated by Braun.

ADMIXTURE OF POTASSIUM SULFATE

A more promising line of research was taken up by Hoffmann and Kochmann[8] and, for dental practice, by Philipp,[9] who found that by the addition of potassium sulfate the concentration of novocain can be reduced to one-half, that of suprarenin to one-fourth of the usual dose. Philipp employs for dental operations the following formula: Novocain 1, L. synthetic suprarenin Hoechst 0.00125, potassium sulfate 0.4, to be added to 100 cc. of an 0.9 per cent. sodium chlorid solution; and he claims for it more rapid, profound, and enduring anesthesia, the possibility of employment of larger doses, innocuity even in cardiacs, the aged, debilitated, and the very young, and almost normal postoperative hemorrhage. We await confirmation of these claims by practical experimentation, and the publication of further clinical data.

ISOTONIA OF SOLUTION

So far, the solution of novocain-suprarenin in modified Ringer solution, as thoroughly tested by Prof. Guerber at the instance of Prof. Guido Fischer, and elaborately discussed in all its phases in the latter's text-book, has proved most advantageous in every respect. A repetition here of the modified Ringer formula may not be amiss:

Sodium chlorid,	0.5
Calcium chlorid,	0.04
Potassium chlorid,	0.02
Aqua destillata	100.00

The very convenient tablet form in which this mixture is being marketed, one tablet to be added to 10 cc. of aqua destillata, is of great practical advantage.

A great deal of discussion has arisen as to the optimum isotonia of normal (physiological) salt solution in combination with from 1-2 to 2 per cent. novocain. Seidel especially has expended a great deal of ingenuity and energy in an effort to arrive at definite conclusions. Yet the discussion of this point at a meeting of specialists in local anesthesia, held at Münster i. W. on November 15 and 16, 1912, resulted in the adoption of the compromise resolutions Nos. XIV and XV, stating that *The question as to what percentage of sodium chlorid should be added to a two or a one per cent. novocain-suprarenin solution in order to make an absolutely isotonic solution is not accurately solved as yet. The data adduced by Bünte, Moral, and Fischer do not seem to be sufficient to guarantee a scientific solution of this question. Practical experience shows no difference whatever in the behavior of 1 1-2 or 2 per cent. novocain solutions in from 0.6 to 0.9 per cent. sodium chlorid solutions. The amount of sodium chlorid which would fulfill also the theoretical requirements is not yet known.*

It is rather surprising that in all these discussions regarding the isotonia of the anesthetic solution, the variances in the chemical composition and the sodium chlorid contents of the blood of various individuals, or of the same individual at different times, as affected by age, illness, or pregnancy, have been left out of consideration. It is manifestly impossible to determine accurately the sodium chlorid factor in the blood of every individual without a previous careful analysis. A low percentage of sodium chlorid, 0.6 per cent., seems preferable, as this percentage is raised slightly by the admixture of the calcium and potassium chlorids in the Ringer solution, and of the novocain, and by the evaporation of water during the routine boiling of the solution before and after the addition of the novocain-suprarenin.

PREPARATION OF THE ANESTHETIC SOLUTION

Great care should be exercised in the acidulation by hydrochloric acid of the normal salt or Ringer solutions, as recommended by Braun. If a receptacle of non-alkaline Jena glass is used, this acidulation is unnecessary. If one of ordinary glass is employed, the operator should make sure that only a minute quantity (one drop) of a very weak (10 per cent.) pure hydrochloric acid solution is used, since any undue excess of the acid will produce considerable after-pain, and possibly tissue lesions.

The method of making a fresh solution from novocain-suprarenin tablets in front of the patient has a great deal to recommend it. By watching, the patient's mind is occupied, the operator has an opportunity to impress the patient with the asepsis of his working method, and the best possible guarantee is assured to both patient and operator as to the injected solution being really sterile.

The employment of the dry novocain-suprarenin tablets for preparing the solution has proved to be most practical in dental practice. Seidel's method of adding the suprarenin in liquid form from a standard pipet admits too many possible sources of error, and will never aid in rendering local anesthesia the common property of dentists. Suprarenin will keep longest in dry form, and the discoloration of the solution is a reliable guide as to its quality. No risk should be taken with a solution made from tablets which are not white. Tablets should be kept in rubber-stoppered tubes preferably. Sometimes a slight discoloration of the topmost tablet in a freshly broached tube is noted; such tablets are to be discarded promptly, and special attention should be paid to the color of the solution of the other tablets in such a tube; they will usually be found absolutely fresh and white.

In fairness to method and operator alike, the manufacturers of novocain-suprarenin tablets should be willing to print the date of manufacture or packing of the tablets upon the tubes, and to use air-proof and bacteria-proof stoppers to insure the freshness and sterility of the tablets. Preservation of the tubes in a dry and cool place will then insure a maximum stability of the tablets, which in my experience have kept fresh in unbroached tubes for two years. After a tube is once opened, its contents should be used up within a reasonably

short time, since the repeated admission of air and moisture soon seems to inaugurate chemical changes.

The addition of sodium chlorid to novocain-suprarenin tablets for the purpose of simplifying the preparation of isotonic solutions, as practiced by some drug houses, should be discouraged, since they give discolored solutions within a very short time after purchase, and especially after a tube has been broached, proving that the combination of novocain-suprarenin and sodium chlorid is very unstable, chiefly owing to the hygroscopic property of sodium chlorid.

AMPULES

The slight disadvantage which may accrue from the hygroscopic nature of novocain-suprarenin tablets is overcome by the use of sterile novocain-suprarenin solution in ampules of neutral yellow Jena glass . For the practitioner who employs local anesthesia only occasionally, this form seems the most practical. The objections to ampules which I have raised before,[11] saying that "Their contents are not always sterile, small openings being left in sealing the glass necks," have been overcome, since reliable manufacturers are now carefully testing in a vacuum each ampule as to its being hermetrically and firmly sealed. In general medical practice, millions of ampules are used every year with apparently perfect safety, and this form of dispensing solutions is increasing in popularity with the growing use of intravenous medication. Moreover, the discoloration of stale novocain-suprarenin solutions is a reliable danger signal. In a busy practice, of course, the routine use of ampules will prove rather expensive.

DANGER FROM STALE SOLUTIONS

The practitioner cannot be too urgently warned to refrain from the use of stale novocain-suprarenin solutions, which may produce very serious results, such as analgesia persisting for weeks, extensive edema, dangerous hemorrhage, and necrosis.[12] Considering the ease with which absolutely safe solutions can be prepared, such sequelæ are inexcusable.

ADMIXTURE OF SUPRARENIN

In accord with several other investigators, Seidel[13] has pointed out that the toxicity of our anesthetic solutions is due less to the novocain than to the suprarenin. Suprarenin is probably the strongest poison known, being active even in a dilution of 1 : 100,000, yet we cannot and would not dispense with in local anesthesia, as it not only localizes and intensifies the action of novocain, hence allows of the concentration of the anesthetic and the injection of larger doses, and produces a temporary anemia so essential for neat surgical work without continual flooding of the field of operation, but, according to the findings of Kochmann and Esch,[14] it prepares the nerve tissue for the reception of the local anesthetic in about the same manner as a mordant is applied in the dyeing industry for rendering cloth more receptive of the dyestuff. Since fractions of one milligram of suprarenin suffice to produce anemia in a comparatively large operative field, the percentage can be reduced without essentially impairing the anesthetic action of the solution, in arterio-sclerotics, cardiacs, suspected aneurysm, in children and the aged, also in those operations in which anemia of the field is not essentially necessary, as in simple extractions, pulp extirpations, excavation of hypersensitive dentin, or scaling operations. In all these cases I have obtained excellent results from tablets E and G—the E tablet containing 0.02 gram novocain and 0.00005 gram suprarenin, the G tablet 0.015 gram novocain and 0.00005 gram suprarenin—by adding from 1-3 to 1-2 more Ringer solution, thus reducing the concentration of both novocain and suprarenin without notably reducing the anesthetic power of the solution.

A tablet of the concentration of 0.02 gram novocain and 0.00002 gram suprarenin was first suggested at the Münster meeting held in November, 1912, and Thoma, of Boston, attributes special advantages to this tablet, which he has christened the T tablet. These advantages, in my opinion, are rather illusory, since the modified tablet E solution does not produce an anemia sufficiently pronounced to interrupt the circulation of the blood completely, and in surgical operations such as specially difficult extractions, apical resections,

or curettages, it is customary to freshen up the wound by suitable manipulation or the use of a sharp spoon so as to produce a free flow of blood before suturing the wound. According to Braun, who surely speaks with authority, the dosage of suprarenin as employed in the tablets designed for dental purposes will not produce any untoward effects. Hospital internes are employing considerably larger doses in collapse due to infectious diseases, as much as 6 mg. per day, even 24 mg. per day (Kirchheim). The doses employed in local anesthesia may therefore be considered innocuous as long as pure and fresh preparations are employed. Euler and Scheff have proved by experiment that the vitality of a dental pulp is not endangered by the now generally adopted dosage of our injecting solutions, and the latter's statement has been verified by innumerable experiments, that the E and G novocain solutions do not in the least disturb either the vitality of the teeth anesthetized or that of the approximating teeth, "*provided the perfect vitality of the pulp before injection has been established.*"

For the sake of systematization, individualization in selected cases, and simplicity of technic, it is highly desirable to adhere to the solutions which have proved so eminently satisfactory in innumerable cases.

The systematic innocuity of our dental solutions has only recently been attested anew by Dr. A. Therre's[15] painstaking investigations in lactating women, who exhibit no subjective symptoms whatever, no changes quantitatively or qualitatively in the milk or urine, or in the behavior and frequency of urination in the child, and no chemical trace of novocain or adrenalin in the mother's milk or urine.

THE MÜNSTER RESOLUTIONS

For the sake of completeness, it may be well to quote here the sixteen resolutions adopted by the Münster meeting, as they represent an important landmark in the controversy concerning the dosage of novocain-suprarenin solutions:

(1) The fresher a novocain-suprarenin solution, the less its toxicity and the greater its anesthetic effect. For this reason, all scientific investigations regarding the effect of these preparations should be conducted exclusively with absolutely fresh solutions prepared and sterilized by the operator himself. A clear idea of the effect of novocain-suprarenin solution can be obtained only if the operator is certain of having used only novocain and suprarenin, not their products of decomposition. Test solutions must not contain any admixtures excepting the amount of sodium chlorid necessary for isotonia, else the possible sequelæ from such admixtures might be confused with those from the novocain and the suprarenin. These factors must not be lost sight of in the judgment of the earlier literature on this subject.

(2) Fresh novocain solutions, as well as fresh suprarenin solutions and fresh mixtures of novocain and suprarenin solutions, must be as clear as water and colorless.

(3) In practice, any novocain solution is to be regarded as being *fresh* and fully effective as long as it remains clear and colorless.

(4) The same applies to suprarenin solution. Solutions of suprarenin are the less stable the more diluted they are.

(5) Novocain and suprarenin solutions in mixture can be considered fresh only directly after mixing the two preparations in solution.

Within ten minutes under certain conditions, such as excessively high temperature, influence of light, or admission of air, discoloration of the novocain-suprarenin solution, with diminution in anesthetic power and increase in toxicity, may occur.

(6) A sterile novocain-suprarenin soluion cannot be rendered more stable by antiseptic admixtures, as the yellow discoloration of the novocain and the red discoloration of the suprarenin is based upon chemic processes—oxidation, not upon bacterial ones.

For this reason a novocain-suprarenin solution must be sterile, but need not be of antiseptic character.

(7) Antiseptic admixtures, as for instance thymol, are not only superfluous, but deleterious. At present no antiseptic is known to exist which in a concentration of sufficient antiseptic power to permit of easier manipulation of the solution, is absolutely non-irritating when injected.

(8) Individualization in the concentration of the novocain is not necessary in the small doses employed in dental operations. Contrary to cocain, it is immaterial whether a certain dose of novocain is injected in weak or strong concentration, as long as the entire dose does not exceed 0.2 gram.

(9) Since in dental operations the part to be anesthetized, the bone of the maxilla and the teeth, cannot be infiltrated directly, but the diffusion of the anesthetic must be relied upon, only solutions of comparatively high concentration are applicable.

(10) The optimum concentration of novocain for dental purposes is the 2 per cent. solution.

(11) On the other hand, the concentration of suprarenin calls for individualization in many cases in dental practice. This is necessary, because—

a. The toxicity of the suprarenin largely depends upon the concentration of the dose employed, especially in aged individuals and arterio-sclerotics, and in case of accidental injection into a bloodvessel.

b. The more nearly normal the hemorrhage from a wound in the oral cavity, the better the course of healing and the less the probability of after-pain. Since in many cases, such as root-resection without skilled assistance, or fractures, a pronounced anemia of the field of operation is desirable, while in other cases, such as easy extractions, normal hemorrhage should be interfered with as little as possible for the sake of rapid wound-healing, therefore, all these circumstances call for individualization in the dosage of suprarenin.

(12) In normal cases, the best results are obtained by the addition of 0.00002 gram suprarenin to each cc. of 2 per cent. novocain solution.

(13) In cardiacs and in the aged this dosage should be reduced to 0.00001 gram; if pronounced anemia in the field of operation is desired, increase to 0.00005 gram.

(14) and (15) (See under Isotonia of Solution).

(16) The above requirements for dental practice are not entirely fulfilled by the percentages contained in either novocain-suprarenin tablets or ampules. The operator, therefore, should prepare and graduate his own solutions in the manner described by Seidel or by some other suitable method.

A further commentary on these resolutions is superfluous, since every phase contained therein is critically discussed in the respective subdivisions of this paper.

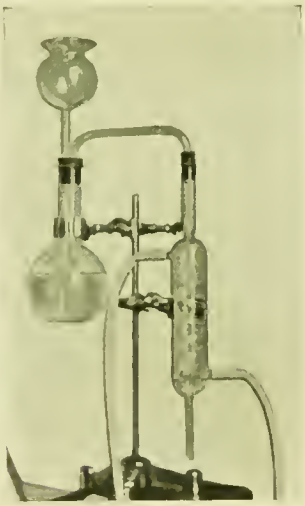

Figure 1. Silverman's apparatus for distilling water.

THE IMPORTANCE OF DISTILLED WATER

Too much attention cannot be paid to the use of really distilled water in preparing the Ringer solution. The shortcomings of the aqua destillata as purchased in pharmacies have been emphasized by me before,[16] and have since been corroborated by analysis of further samples bought at random. As a home-made filter, the one suggested by W Merres[17] will suffice for small quantities. But recently a far more elegant apparatus has been constructed by Dr. S. L. Silverman, of Atlanta, Ga., which has a capacity of eight ounces (See Figure 1); but a Femel, Boltze, or other distilling apparatus will prove a decidedly good investment to the practitioner who does not care to construct one of these appliances himself.

MODIFICATIONS IN THE INSTRUMENTARIUM SUGGESTED

This brings us to the question of instrumentarium, in regard to which I have offered the following suggestions to the section on Anesthesia, of the Sixth International Dental Congress, London.

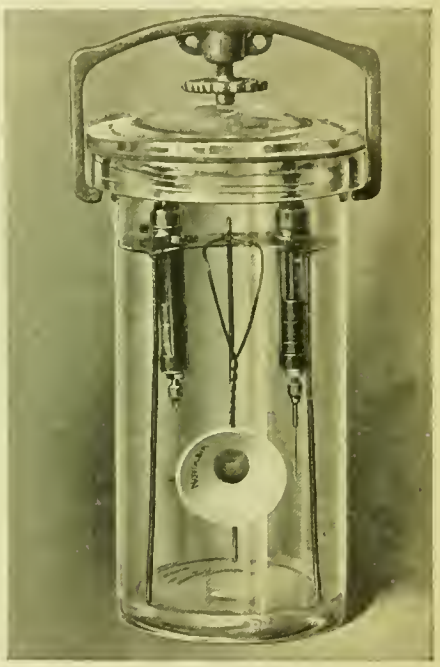

Figure 2. Author's anatomic specimen jar for preserving syringes, dissolving cups, pliers and lancet.

Fischer has shown that every instrumentarium should be designed with a view to avoiding any break in the delicate chain of asepsis. With this aim in view, I have suggested a slight modification of his instrument jar. An anatomic speciment jar (See Figure 2) is fitted with a platform-stand of porcelain, glass, or enamel ware, accommodating two Fischer syringes fully mounted, one with a short, the other with a long needle, and corresponding hubs, a graduated dissolving cup of porcelain, a pair of aluminum tweezers—that metal not being attacked by the action of iodin—and two reserve

needles and hubs. In this jar the sterilized instruments are suspended in a mixture of 70 per cent. alcohol one-half gallon, and chemically pure glycerin about one fluidounce. The glycerin is added merely for the purpose of imparting to the alcohol a slightly lubricating quality. Alcohol in the strength of from 60 to 70 per cent. has the greatest germicidal power according to the findings of Leedham-Greene[18] and Beyer.[19] Post and Nicoll claim germicidal power for solutions as weak as 30 per cent., while, on the other hand, Koch's and Sternberg's experiments have shown that chemically pure alcohol and 95 per cent. alcohol is without germicidal effect. The mixture indicated by Fischer, of two parts absolute alcohol and one part glycerin, makes the instruments very disagreeable to the touch, and slippery, if the glycerin has not been completely washed off; it also requires a more lengthy and tedious washing in boiling sterilized water to remove all traces of the preserving solution, which, if injected hypodermically with the novocain-suprarenin solution, would produce most undesirably prolonged anesthesia.

The boiling water drawn up into the syringe to rinse out the alcohol and glycerin should never be squirted back into the sterilizer, since by doing so the water in the sterilizer is mixed with traces of glycerin, and the anterior of the syringe barrel really is not freed entirely from this undesirable admixture.

Clamping of the cross-bar to the rubber ring fitting to the edge of the jar prevents all ingress of air, dust, and bacteria, also the sticking of the lid so often encountered if ground-glass covers are used, as well as evaporation of the alcohol.

I have also suggested another jar, in which the ground cover can be easily pried loose even in case of sticking, and which is more elegant than the anatomic specimen jar.

A platform of glass, porcelain, or enamel ware is being suggested for the reason that aluminum, or nickeled metal, soon oxidizes, especially if the stand is not fully immersed in the alcohol. If a metal stand is used, the alcohol should be poured away, the stand cleaned, and a new alcohol solution made as soon as the old one appears cloudy. In order to prolong the usefulness of the solution, which gradually loses its optimum concentration owing to its hygroscopic nature, it is practical, when the syringe is put away after use, to rinse it thoroughly inside and out in boiling distilled water, and then to evaporate the adhering water in dry heat, as for instance by laying the syringe on a sterile napkin on top of the closed sterilizer. Care is to be exercised not to overheat the syringe, and to allow it to cool somewhat before drawing into it any alcohol solution from the jar, and suspending it in the mixture, lest the glass barrel crack.

The electric sterilizer or boiler, which is best fed with distilled water, should be so constructed that the heating elements do not come into direct contact with the water. Sterilizers so constructed that the heating element dips into the water are unsuitable, as they are unclean at best. The use of gas-burners is not advisable, as the combustion is not perfect unless compressed air is admixed, and undesirable particles of soot are carried into the solution or deposited upon the iridio-platinum needle in sterilizing by blowing it out in the flame.

It is perhaps no unnecessary repetition to point out again that all alkalis, such as the soda admixture customary in sterilizing instruments, must be religiously avoided, since even minute traces of alkalis have an untoward effect upon novocain-suprarenin solutions, as they precipitate the novocain in the form of the base, which is insoluble in water, the tablet consisting of the hydrochlorid of novocain.

The use of saturated borax solution for preserving the syringes I have found unsatisfactory as the metal parts are quickly oxidized and borax in substance is deposited thereon. Even in the alcohol solution, oxidation of the metal parts of the syringe will take place after a while, so that occasional cleansing and sterilizing of the syringe is indispensable. The more deeply the syringes dip into the alcohol mixture, the greater the guarantee that they will be sterile when removed therefrom, and that no contamination of the solution with bacteria collected on the outside of the syringe can take place.

I am at present conducting a series of experiments with white liquid vaselin as a medium in which to preserve syringes, and hypodermic needles, in sterile condition. From evidence gained so far, this or similar media will offer

Figure 3. Author's improved container for Ringer Solution.

considerable advantages over alcohol. A more definite verdict, however, must be reserved for a future paper, as a great many bacteriological and other tests will have to be made before any decision can be reached as to the advisability of the adoption of these petroleum products for the purpose indicated.

glass cover. If a quantity of solution is desired, the cover is turned to make the two holes coincide and admit a minimum of air, which additionally can be filtered by fastening a pledget of sterile cotton over the hole in the neck by means of a rubber band, or dental floss. To emit the liquid it is further necessary to turn the glass cock so as to bring the perforation therein in line with the aperture in the nozzle. Immediately after the desired amount of liquid has been poured out, the glass cock is given a turn of 90 degrees, and the cover is turned slightly in the neck of the bottle, thus excluding all air while the solution is not needed. When the flask is not in use, the aperture of the nozzle must be protected against dust by inserting a wisp of sterile cotton. This drawback is overcome in the flask illustrated in Figure 3, also of my design, made of non-alkaline glass. Its construction is based on the principles just described. Instead of a glass cock, a glass hood is fitted over the nozzle so as to exclude all air when the flask is not in use. I have found Ringer solution to remain sterile in this container, which is made in 50 or 100 cc. sizes, for over a month. It is advisable, of course, to make a small and fresh quantity of Ringer solution from the Ringer tablets every week. Like the tubes containing the novocain-suprarenin tablets, those with the Ringer tablets must be carefully stoppered immediately after the required number of tablets have been rolled out, since they are highly hygroscopic. None

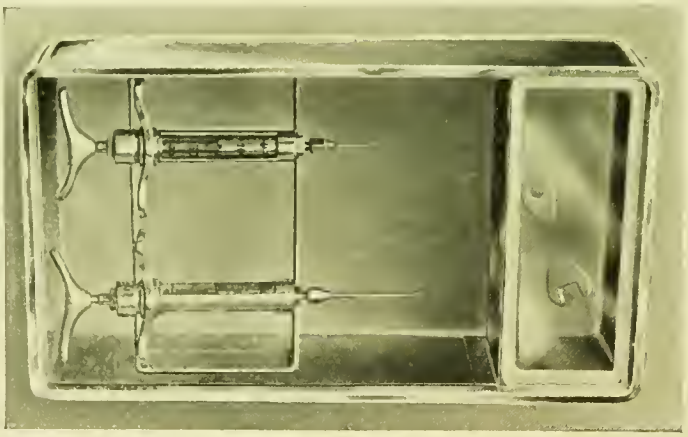

Figure 4. Author's working tray of glass

STOCK FLASK FOR RINGER SOLUTION

For preparing, preserving, and dispensing the Ringer solution under as nearly bacteria-proof conditions as possible, I have designed two receptacles. One has a small pinhole opening in the side of the neck, as does the ground-

of these tablets should ever be touched with the hand; they can easily be rolled out of the original tube into the liquid in which they are to be dissolved, and a probable source of contamination is thus easily avoided.

To prevent possible breaking of the stock flask when preparing and sterilizing the Ringer solution, a sterile napkin, or a wad of sterile cotton is wound around the flask, and the flask is set into the water of the sterilizer before the current has been turned on. The glass stoppers also are sterilized by boiling, the large opening in the flask having been stoppered with a wad of sterile cotton. Sterilization of the Ringer solution is imperative, though fresh tablets and aqua destillata have been used, and sterilization can be considered complete after the flask has stood in this improvised water-bath for about twenty minutes. The ground-glass stoppers are put in place upon completion of sterilization with a pair of sterile pliers, and the flask is allowed to cool. Fractional sterilization of the Ringer solution is ideal, but impractical. Moreover, the boiling of the solution before adding novocain-suprarenin tablets insures perfect sterility.

GLASS WORKING TRAY

A working tray of glass with aluminum inset (See Figure 4), on which the syringes with either long or short needles and hubs can be safely deposited while not in use, has proved to be a valuable accessory, as it prevents accidental contamination of the needle or syringe, blunting of the needle, and injury to the operator. The measurements of this tray are such as to accommodate the syringes when filled. The tray is additionally fitted with a smaller tray with ground-glass cover for keeping needles, hubs, wrench, broaches, and probes in an antiseptic solution. Below the inset there is sufficient space for depositing a Pravaz syringe outfit, ampules containing camphorated oil for hypodermic use, amyl nitrite, and a small bottle of camphorated validol, all of which prove invaluable if close at hand when needed. I have never had to use any but the camphorated validol, of which I administer five drops in a little water to children, ten drops to adults, as soon as the slightest trace of facial pallor appears, which usually is due to nothing more than fear, or, in difficult extractions, to mental and physical strain. A tube of bromural tablets, for internal administration to fretful children and nervous adults, 30 minutes before injection, one of trigemin capsules to be given with proper instructions to patients in whom, owing to the severity of the operation and the resulting surgical traumatism, post-operative pain is to be expected, and one of novocain powder to dress wounds with so as to insure speedier and painless healing, are also always kept close at hand.

NEEDLES

The possibility of breaking a needle during the act of injecting still deters some operators from adopting local anesthesia in their practices. This danger has been largely done away with by the use of iridio-platinum or tantalum in their manufacture. Steel needles do not permit of sterilization by drawing through an alcohol flame; hence, unless such a needle has been thoroughly boiled immediately before injecting, we are never sure as to its sterility. Owing to the danger of rusting, steel needles should be discarded immediately after use. The inexperienced operator especially should not attempt to acquire facility in injection with the use of these needles, fragments of which are difficult to remove, especially if the needle has broken in conductive work. If, in simple infiltration anesthesias, where, owing to the resistance of the periosteum a needle is more liable to break, especially if excessive pressure is employed, the operator fixes his palpating finger-tip over the needle point, as a routine manipulation, compression with this finger-tip will prevent disappearance of the needle fragment into the soft tissue; after more or less complete anesthesia has been established, depending upon how much solution has been injected before the accident occurred, the fragment is located by a transverse (never a vertical) incision with a sharp, sterile lancet, and picked out with sterile pliers. Iridio-platinum needles have given the best service; they are sterilized in the alcohol flame before the solution is drawn into the syringe, and before putting the syringe away in the alcohol jar. If the point has become dull, it can easily be freshened with a fine stone in the dental en-

gine. Excessive sharpness of the point is as undesirable as dullness; the former because blood vessels might be pierced instead of being gently pushed aside, the latter because the undue pain from the insertion of the needle might frighten the patient, and lacerations of the more deeply lying tissues might be produced.

The experiments with trocar needles as suggested by Fischer are not yet final. If a trocar needle is employed, it is necessary to wait until the cannula has filled entirely with blood, otherwise there is danger of causing an air embolus. In conductive anesthesia in the mouth, where we usually injure no blood vessels, hence cause

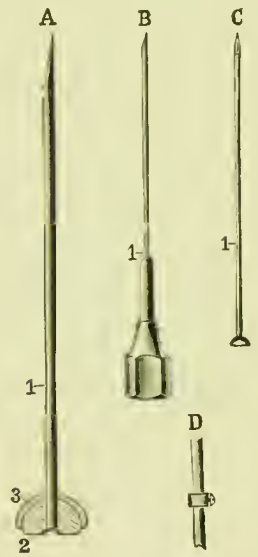

Figure 5. Suggested improvements in iridio-platinum hypodermic needles.

A, Enlarged reproduction of needle. 1, Point of taper. 2, Soft metal core for tightening the needle on the orifice of the syringe. 3, Conical outer shell of hard metal.

B, Long needle with taper at 1 in long hub.

C, Long needle with taper at 1 for conductive work; length 42 mm., diameter 0.47 mm.

D, Safety device with set-screw applied just above the taper of the needle.

little or no hemorrhage, it may require some time till the cannula fills. At any rate, the straight needle technic has proved so simple and satisfactory that it may be wise to consider this as the standard method until a really remarkable improvement has been suggested, which is hardly likely to occur.

An important step toward greater safety, however, could be made, if the manufacturers of hypodermic needles would construct their needles on the principle of the Gates-Gliddon or Beutelrock drill, with a slight taper toward a shoulder which would come to lie just outside of the mouth of the hub (See Figure 5), so that, if a break should occur, it would be likely at this weakest point, leaving a portion of the needle protruding from the mucous membrane, and making it possible by swift manipulation to withdraw the fragment with a pair of sterile pliers without any incision. The best safeguard against breaking a needle is, of course, delicate manual dexterity, and the avoidance of all undue force or pressure.

To allay the novice's fear of breaking a needle, I have thought of the safety device illustrated in Figure 5, D. This consists of a delicate iridio-platinum ring with set-screw which is fastened on the needle just above the taper. Owing to its smallness, it will not interfere with the manipulation of the needle, which should be of slightly greater length to allow for the slight loss in reach occasioned by the safety device. If the needle should now break, which is most likely to occur at its weakest point, viz., the taper, it cannot escape into the tissues, the diameter of the safety device being larger than that of the needle puncture, and the needle can be easily picked out before it has any opportunity to migrate.

PROPOSED MODIFICATION IN THE FISCHER SYRINGE

Since Bolton[20] has shown by very painstaking tests that the metal parts with which the novocain solution comes in contact within the Fischer syringe act as electrodes, the solution itself as an electrolyte, producing fairly rapid decomposition of the solution, as evinced by its discoloration if left in the syringe barrel for more than about ten minutes, it seems advisable to cover these metal parts with an insulating layer of cemented glass, or better still, some form of insoluble enamel which would not materially complicate the manufacture of these beautiful instruments.

PREPARATION OF THE FIELD OF INJECTION

Next in importance to the sterility of the anesthetic solution and the instrumentarium is the preparation of the field of injection.

While it is manifestly impossible to sterilize the oral cavity, we can always succeed in sanitation of the mouth and in rendering the micro-organisms innocuous for a sufficient length of time to allow the introduction of the anesthetic solution without contamination. Spraying of the patient's mouth with a mildly antiseptic solution of pleasant taste or with normal salt solution delivered by a compressed-air atomizer, which should be a routine measure preceding any dental operation, is especially indicated in the practice of local anesthesia.

To prevent the introduction of micro-organisms or their toxins from the mucosa into the deeper strata of tissues, Fischer, in compliance with a generally followed surgical practice, recommends the application of iodin and aconite, equal parts, upon the previously dried mucous membrane. The aconite, however, imparts hardly any virtue to the iodin, since aconite has no value as a disinfectant, and its depressant effect upon the peripheral sensory nerves requires some time to become established. On the other hand, aconite is highly toxic, and when introduced into a wound produces a peculiar constitutional effect. The Dispensatory of the United States distinctly warns that "Care should be taken not to apply aconitin to an abraded surface or to mucous membrane, for fear of poisoning." Consesidering these drawbacks, which have been pointed out also by Camnitzer[21] and Blaaberg,[22] and for which the theoretically correct but practically slow anesthetic action of aconite on the mucous membrane in no way compensates, the omission of aconite is not only justified, but desirable.

Even in the application of tincture of iodin to the mucous membrane, in analogy with its routine application in surgery preceding incision into the skin, judgment is required. In the first place, tincture of iodin deteriorates very rapidly, forming hydriodic acid; hence, as Abel states it,[23] one week after preparation it becomes an irritant, and after one month a caustic, destroying the epidermis. Again, in children and delicate persons even fresh tincture of iodin sometimes produces blistering and ulcers; and lastly, the patient may have an idiosyncrasy for iodin. An interesting treatise on "The Local Preparation of Patients for Operation," by A. D. Whiting, M.D., in this connection deserves special mention. G. Zanetti[26] found, after testing various substances as a vehicle for iodin, that benzol dissolves iodin rapidly, and the solution keeps indefinitely, while the benzol seems to enable the iodin to penetrate more deeply. The saturated solution contains 9.75 per cent. iodin, while tincture of iodin represents less than this.

Decolorized iodin in the form of diodohydroxy-propane, or iothion, has the advantage of containing up to 70 per cent. iodin in combination with alcohol and glycerin; it penetrates the gingivæ more deeply without damaging the mucosa, and is applicable even in cases of pronounced idiosyncrasy for iodin. I have found it to be of great value also in cases of periosteitis, stomatitis, and gingivitis, and the cleanliness of its application and freedom from decomposition render it preferable to ordinary tincture of iodin in all dental operations.[27]

Decolorized iodin, moreover, facilitates the observation of the gradual advance of anemia of the gingivæ following infiltration, which, to the trained eye, is a valuable symptom for guaging the depth of the anesthesia. Moreover, the break in the chain of asepsis, which is so often made my practitioners who merely wash their hands with water and soap before making an injection, is prevented if the operator's palpating finger or preferably his hands are painted with iothion in olive oil. This form of sterilization also augments the delicacy of the sense of touch, and is therefore preferable to the application of collodion for this purpose as suggested by Bolten-Husum.[28]

For the beginner in local anesthesia, however, the iodo-benzol seems preferable until the individual steps of the technic have become routine practice, as by its color it indicates the fact that the sterilization of the mucosa has not been overlooked, and marks the area for insertion of the hypodermic needle. Iodo-benzol, moreover, by its slightly escharotic action and burning disguises the slight pain incident to the needle prick, which, for very excitable patients, should be rendered entirely painless by swabbing the place of injection with 30 per cent. pure novocain solution or by dissolving and distributing by rubbing with a large ball-burnisher a novocain-suprarenin pluglet as used in pressure anesthesia. Great care is necessary not to apply too much iodo-benzol,

as any surplus reaching the soft palate, tonsils or back of the tongue will set up an extremely disagreeable irritation.

Following Dr. J. E. Nyman's[29] suggestion, I have, for some time, employed the following iodin preparation with great satisfaction: *Iodin crystals, menthol crystals, equal parts, dissolved in benzol.* The menthol disguises the benzol odor and acts as a refrigerant anesthetic upon the mucosa, thus completely disguising the needle prick.

PRESSURE ANESTHESIA FOR THE EXTIRPATION OF PULPS

While absolutely painless extirpation of the pulp can be achieved very easily either by infiltration or conductive anesthesia, the technic of pressure anesthesia as familiar for years with cocain can be most advantageously employed by using the novocain-suprarenin pluglets especially designed for this purpose. For confining the anesthetic in the cavity and distributing the pressure evenly, unvulcanized weighted rubber is preferable to ordinary unvulcanized rubber. These pluglets are also of great service in densensitizing hypersensitive dentin, the hypersensitive area being dried and one pluglet being vigorously rubbed into it with a ball burnisher moistened with oil of cloves.

Since the question as to who first suggested the method of pulp extirpation by cocain-pressure anesthesia still seems to be a mooted one, it may not be amiss in this connection to review the evidence. In a "Symposium on the Removal of Pulps," held by the Odontographic Society of Chicago, on January 16, 1905, Dr. L. L. Funk,[30] of Chicago, reported that early in 1892, after various experiments with cocain, one of which was for the desensitization of a wart on his own knuckle, in which pressure was exerted on a pluglet of cotton saturated with a 10 per cent. solution of cocain by a rubber tube placed over the stem of a chip blower, it occurred to him that "*a cavity in a tooth was advantageous to this operation, from the fact that the walls of the cavity would confine the medicine.*" Subsequently he "*placed the cocain in the cavity, covered it with a piece of soft, rubber, using a burnisher to force the cocain in, and took the pulp out without pain.*"

Dr. Edward C. Briggs,[31] in 1892, described his method, which consisted in exposing the pulp, then applying on cotton some freshly prepared 20 per cent. solution of cocain hydrochlorid. With a hypodermic syringe, mounted with the point of a Dunn syringe, gradual pressure was exerted over the point of exposure, "*carrying the solution up and around the pulp to its extreme end.*" Apparently the first full description of the method now in vogue, which is essentially that of Dr. Funk, was given by Dr. B. S. Hert,[32] of Rochester, in March, 1902, in a paper on "Cocain in Pulp Extirpation," the writer claiming no originality, saying "It is almost two years since I learned of this manner of using cocain."

THE TECHNIC OF INJECTION

The technic of injection is entirely based upon anatomic considerations which, for our special purpose, have been worked out in detail by Braun, Fischer, and the latter's former assistants, Brünte and Moral. It lies outside the scope of this paper to repeat the anatomic description of our field, except as far as some disputed points are concerned. Any text-book on anatomy in general, or on local anesthesia in special, also many of the essays which have appeared within recent years in American dental journals, offer ample information on this phase, though it should be remembered that a great many writers offer the findings of Braun and Fischer as their own, according to the most reprehensible habit of many dental writers who invariably fail to give credit where credit is due. In the following, an attempt will be made to tabulate in a terse manner the various factors that make toward a successful application of local anesthesia.

INFILTRATION OR MUCOUS ANESTHESIA

The maxilla, owing to the liberal distribution of spongiose, greatly canaliculated, or cancellated areas throughout its superficial cortical layer both facially and palatally, lends itself most favorably to mucous or infiltration anesthesia, allowing of the ready anesthetization of each individual upper tooth, at any age. In the mandible the cortical layer prevails, increasing in general distribution and density with advancing age, so that infiltration anesthesia is uniformly successful only in children up to twelve years of age,

while in persons above twelve years this method is applicable only for the anesthetization of the centrals and laterals, the osseous environment of which teeth to some extent retains its cancellated character. The mandible, therefore, may be said to be the field *par excellence* for conductive anesthesia, especially since it is difficult to make an injection in the lingual surface owing to the continuous interference by the tongue and the continual inundation of the field of injection by saliva from the sublingual glands.

Infiltration or mucous anesthesia is best accomplished by using the short needle of 23 millimeter length and 0.47 diameter in the short hub, though, after some practice, the operator will acquire sufficient skill to enable him to use the long needle of 42 millimeter length and 0,47 millimeter diameter for infiltration as well as for conductive anesthesia. With the patient sitting erect for injection labio-buccally (dental anesthesia), or greatly reclined for injection palatally (surgical anesthesia), the operator, standing in front of the patient, inserts the needle half-way between the cervical margin and the probable root-apex of the tooth mesially to its long axis at as nearly a right angle as possible to the bone, holding the syringe around the barrel in penholder fashion, and then penetrates with the needle to the bone—this being the shortest, hence least painful, way to the periosteum. He then retraces his fingers along the syringe barrel so that the second and third fingers come to lie against the cross-bar, the thumb over the crutch-shaped handle of the syringe, and injects two or three drops of solution. As soon as a slight whitening indicates the establishment of anesthesia around the point of insertion of the needle, the barrel is declined and the needle is very slowly advanced toward the supposed apical root-end of the tooth to be anesthetized, a drop of solution being pushed ahead of the needle-point so that its advance takes place only in fully anesthetized hence insensible tissue. The advance of the needle must be very slow, else a wheal will be raised: if this occurs it must be immediately distributed by the palpating index finger of the free hand, which continually rests over the advancing needle-point as a control, while the free fingers retract the lip to afford an unobstructed field of vision. The bulk of solution is deposited at the point nearest the root-apex of the tooth.

While infiltration anesthesia has been practiced longer in dentistry, it is by no means easier than conductive anesthesia; the injection requires a much longer time, the liability to causing some pain and tissue lesions, hence after-pain, is far greater, and the anesthesia does not last so long. Moreover, the danger of injecting into a hidden focus of quiescent chronic infection is ever present. Therefore, rather than running the risk of spreading such local infection, conductive or nitrous oxid-oxygen anesthesia should be resorted to in cases suspected or unsuspected, unless a perfectly interprettable radiogram guaranteeing the presence of normal tissue is available. A very instructive illustration of a local infection being spread systematically by infiltration in a pyorrheal mouth is furnished by J. S. Marshall,[33] though this writer wrongly attributes the toxic symptoms to the anesthetic, making—for an author of a dental text book—the astonishing remark, that the patient, who was no other than that writer himself, was enjoying perfect health. We surely have, within recent years, come to regard the presence of pyorrhea of any degree in any mouth as a serious disorder, and the symptoms reported by Marshall are unmistakably pathognomonic of septicemia.

DENTAL VS. SURGICAL ANESTHESIA

The description just given of the technic of infiltration anesthesia applies to anesthesia for dental purposes, the extirpation of a pulp, the excavation of hypersensitive dentin in cavity preparation, or the preparation of a vital abutment in crown and bridge work. This aim is attained by the anesthetic solution paralyzing for a time the sensory nerve branches and terminals in the mucosa, gingivæ, and periosteum on the labio-buccal side, and the pericementum, alveolus, and pulp of the tooth injected. In order to obtain surgical anesthesia, however, for the purpose of extraction, curettage, alveolotomy, or any surgical operation, sensation in the palatal and lingual mucous membrane, gingivæ, and perosteum, as furnished in the maxilla by the posterior and anterior palatine nerves respectively, and in the mandible by the

lingual nerve, must be abolished. This is achieved by injecting a few drops of solution about one centimeter above the cervical margin palatally of the tooth to be operated on surgically. Again the needle is introduced at as nearly a right angle as possible. No further advancement of the needle is needed, as the palatine surface of the alvelous is far more richly cancellated than the facial portion, and anesthesia is very quickly established as evidenced by the rapid appearance and spread of the anemic area. This injection palatally is indispensable in surgical operations, as defined, since encroachment upon tissue innervated by the palatine or lingual nerves will cause pain, hence entirely defeat the object of painlessness so far as the patient's feelings are concerned. The purpose of the proposed operation, therefore, its purely dental or surgical nature, must determine the procedure of injection.

ADJUVANT PRESSURE ANESTHESIA IN PULP EXTIRPATION

In infiltration anesthesia for the extirpation of the pulp in upper molars, it sometimes happens that the pulp in the palatal root retains some degree of sensitivity. It is therefore advisable, in these teeth, either to employ infiltration palatally, or to resort to adjuvant pressure anesthesia. This requires very little more time, and insures entire painlessness, the main object, painless opening into the pulp chamber, which is the part of the precedure most dreaded by the patient, always being obtained by infiltration. The adjuvant application of pressure anesthesia in pulp extirpation is also sometimes indicated when slight sensitivity is left in the root-canal portions of pulps in teeth which have been anesthetized, several at once, by conductive anesthesia, the nerve terminals in the dental pulp seemingly retaining sensitivity the longest. After extirpation of the pulp, which with clever manipulation of the pulp extractor comes away in bulk, the root-canal should be completely cleansed of all the accessory fibrils which can be reached, and dressed with campho-phénique, otherwise sensitivity may be encountered at the next sitting, evidently owing to irritation of the telo-neurons remaining vital in the dentin.

CONDUCTIVE ANESTHESIA

While infiltration anesthesia is essentially of a terminal or peripheral nature, conductive anesthesia aims to intercept or block at a convenient point a sensory nerve before it reaches and distributes itself in the area which its branches supply with sensation. For our purposes, fortunately, it is unnecessary to carry our solution directly into the nerve trunk, make an endoneural injection, as applied in general surgery, since the nerve branches in our special field are slender enough to absorb and conduct the novocain-suprarenin solution, for which they exhibit a peculiar avidity. If the correct technic of perineal injection is followed, therefore, the puncturing of nerve trunks, with subsequent temporary or permanent paralysis of the punctured nerve, should not occur. Such an accident is all the more inexcusable, since our depots of solution are laid in the vicinity of foramina with a liberal super-layer of fatty and connective tissue into which the nerve as well as any blood vessels have ample space to escape, unless the needle is inserted with an unduly fast stabbing motion. By holding the syringe barrel in penholder fashion, and advancing the needle on the surface of the bone in the manner of a delicate probe, and injecting with a slight in-and-out motion, such accidents can be entirely precluded. If paralysis of a nerve should occur, stimulation by daily massage and electric treatment will hasten the regeneration of the nerve. Similar treatment combined with local absorbent medication is indicated in case of puncture of a blood-vessel with subsequent extravasation of blood as evidenced by discoloration. Absolute asepsis of the needle and solution are ideal guarantees against complications in such eventualities—of which, fortunately, but a small number have so far been reported.

The technic of conductive anesthesia is best acquired by practice on green skulls, which are injected with a staining solution and subsequently dissected. In this way the operator acquire a thorough knowledge of the anatomy of the field of injection and operation, of the diffusion of the solution in the tissues, and invaluable confidence. It is also good practice to reconstruct the gingival tissue in a dry skull with wax, up to the reflection of the mucous

membrane, and to acquire in this way a familiarity with the points of insertion of the needle and the manner of advancing upon the surface of the bone. (See Figures 6 to 9). The foramina to be considered in conductive anesthesia, the landmarks for the correct location of the needle puncture, the direction and depth of the advance of the needle of 42 millimeter length in the long hub, the position of the patient's head and mouth, and the quantities of solution injected, are indicated in the following brief directions. In regard to the quantities of anesthetic solution, it should be remembered that the more perfect the operator's technic the less solution will be required to obtain anesthesia.

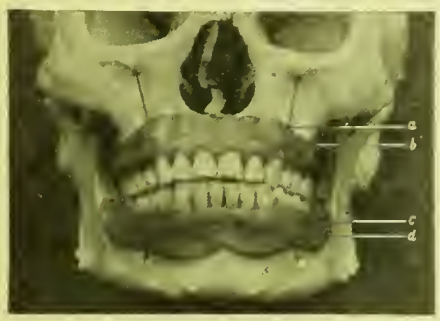

Figure 6. Gingivæ up to reflection of mucous membrane reproduced in wax, (also Figures 7, 8, and9). *a*, Insertion and line of advance of needle for infra-orbital injection. *b*, Point of insertion of needle for tuberosity injection. *c*, Point of insertion of needle for buccinator injection. *d*, Insertion and line of advance for mental injection.

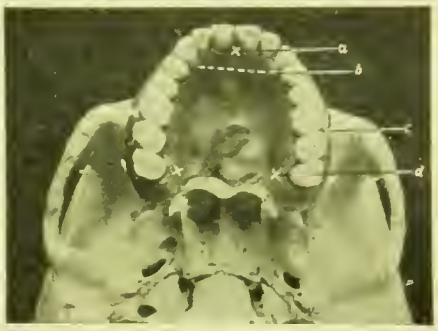

Figure 7. Palatine surface (surgical anesthesia). *a*, Point of insertion of needle for naso-palatine nerve. *b*, Line of demarcation between areas supplied by naso-palatine and anterior palatine nerves. *c*, Point of insertion of needle for tuberosity injection. *d*, Point of insertion of needle for anterior nerve.

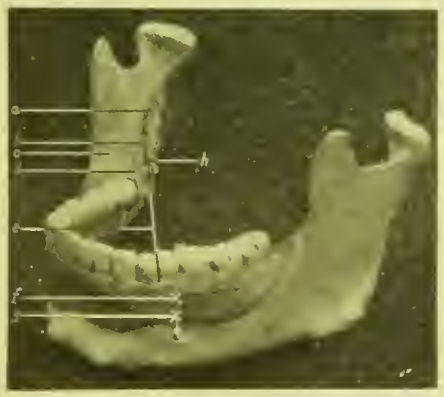

Figure 8. Injections in the mandible. *a*, Pterygo-mandibular sulcus. *b*, Lingula over which the needle should glide. *c*, *d*, External and internal oblique lines forming retro-molar triangle. *e*, Direction of needle for mandibular injection. f, Point of injection and direction of needle for buccinator injection. *g*, Ditto for mental injection. *h*, Depth of needle for injection of lingual nerve, (line foreshortened).

Figure 9. Lingual aspect of mandible. *a*, Direction of needle and syringe for mandibular inpection. *b*, Direction of needle for extraoral injection of mandibular nerve.

BRIEF DIRECTIONS FOR CONDUCTIVE ANESTHESIA

FORAMINA--ANATOMIC LANDMARKS--ADVANCE OF NEEDLE—MANIPULATION OF PATIENT'S MOUTH—QUANTITY OF ANESTHETIC SOLUTION

MAXILLA—FACIAL SURFACE

(1) *Posterior and middle superior alveolar foramina*, located back of maxillary tuberosity below and behind zygoma, giving passage to posterior and middle superior alveolar nerves innervating soft tissues facially, bone and

pulps at first, second, and third molars, and first and second bicuspids. (See Figures 6, 7, 10, 14).

The needle is inserted in the reflection of mucous membrane back of distal root of first molar, and advanced, on bony surface—without discharging solution—in an upward, backward, and inward direction. When the needle is inserted to full length, 3-4 of the contents of the syringe are discharged. If the bicuspids also are to be anesthetized, the remaining 1-4 of the syringe contents is discharged as the needle is withdrawn. Patient's head reclined, mouth closed, cheek retracted. Quantity of solution: 2 cc. (full syringe).

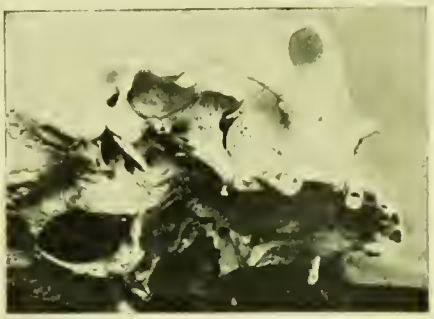

Figure 10. Side view of skull showing pterygo-palatine canal, cribiform plate where the posterior and sometimes the middle superior alveolar nerves enter the body of the bone. Method of tuberosity and infra-orbital injection indicated by arrows.

(2) *Infra-orbital foramen,* emitting *anterior superior alveolar branch* innervating soft tissues facially, bone and pulps of central, lateral, and canine. Owing to anastomosis with the middle superior alveolar branch the first bicuspid also is usually anesthetized. Palpate lower border of orbit on face, press index finger-tip over infra-orbital foramen. Needle inserted in reflection of mucous membrane distally to canine root, advancing needle to about one-half its length while continually discharging solution until felt under palpating finger-tip. (See Figures 6, 10, and 11). Patient's head reclined, mouth closed, upper lip retracted with thumb. Quantity of solution: 1.00 cc. to 1.25 cc. (one-half to three-quarter syringe).

MAXILLA—PALATAL SURFACE

(1) *Posterior palatine foramen,* located in palate on line joining last molar teeth present, emitting *anterior palatine nerve,* innervating soft tissues palatally from third molar to first bicuspid inclusive. Needle inserted as for infiltration of palatal root of last molar, then advanced slightly toward foramen, while discharging drops of solution. (See Figure 7). Danger of going too deeply and directly into foramen. Patient's head reclined, mouth wide open. Quantity of solution: 0.25 cc. (1-8 of syringe).

(2) *Anterior palatine or incisive foramen,*

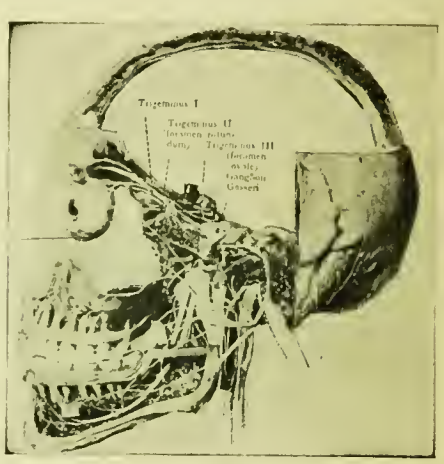

Figure 11. Distribution of the trigemial nerve. Horizontal line indicates the foramen rotundum, (Hirschel).

located in median line back of incisive papilla, emitting *naso-palatine nerve,* innervating soft tissues palatally from canine to canine. (See Figure 7). Needle inserted a short distance anteriorly to incisive papilla, injecting under light pressure, advancing cautiously and slowly to a short distance posteriorly. Patient's head reclined, mouth wide open. Quantity of solution: 0.25 cc. (1-8 of syringe).

MANDIBLE—LINGUAL SURFACE

(1) *Mandibular foramen,* in internal surface of ascending ramus, giving entrance to *mandibular nerve* into mandibular canal, innervating soft tissues facially (mostly), bone and pulps of all teeth from third molar to cen-

tral incisor. From first bicuspid to central incisor, however, innervation by anastomosis from the opposite side must be reckoned with, on opposite side. External oblique line is palpated in mouth, and tip of index finger held in *retromolar triangle*.. Needle inserted at mid-

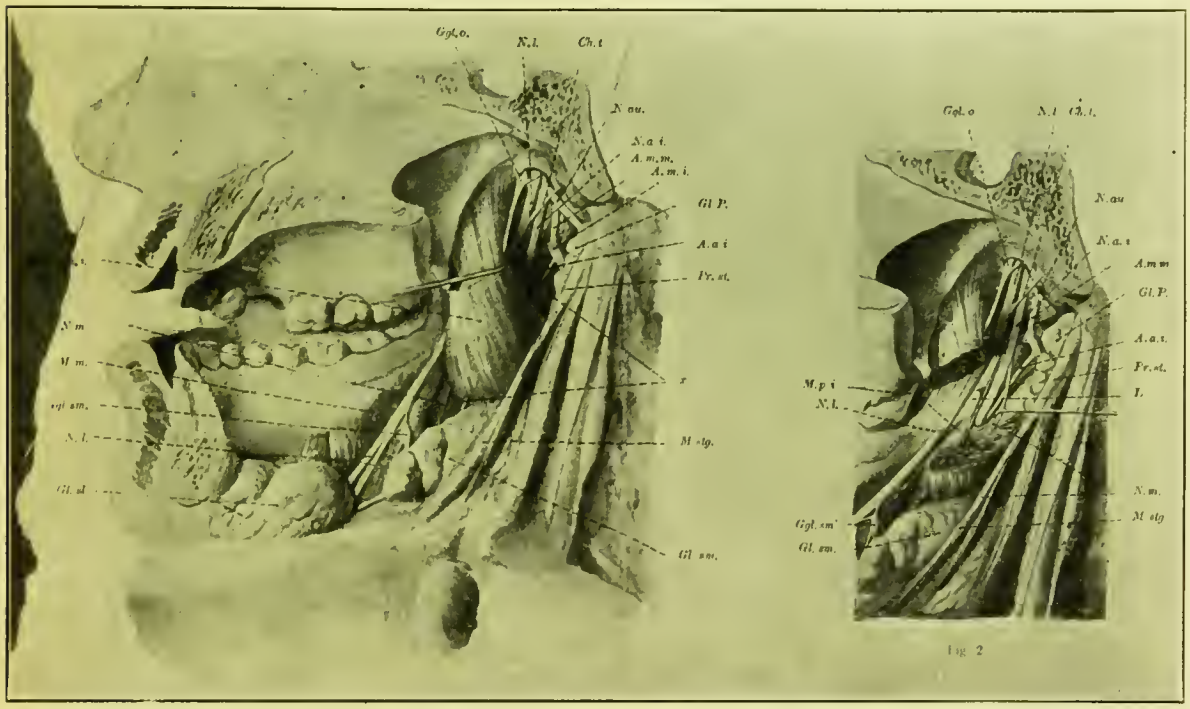

Figure 12, 13. *A. a. i.*, inferior dental artery; *A. m. i.*, internal maxillary artery; *A. m. m.*, middle meningeal artery; *Ch. t.*, chorda tympani; *Ggl. o.*, otic ganglion; *Ggl. sm.*, submaxillary ganglion; *Gl. p.*, parotid gland; *Gl. sl.*, sublingual gland; *M. m.*, mylohoid muscle; *M. p. i.*, internal pterygoid muscle; *M. stg.*, styloglossus muscle; *N. a. i.*, inferior dental nerve; *N. au.*, auriculo temporal nedve; *N. l.*, lingual nerve (greatly stretched); *N. m.*, mylohyoid nerve; *Pr. st.*, styloid process; *X*, hypodermic needle. (13) *L.* Lingual; all other abbreviations as in Figure 12.

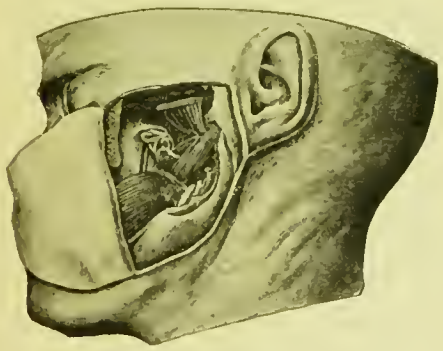

Figure 14. Topography of the maxillary tuberosity with special consideration of the nerves and blood vessels of the ascending ramus, (Gasser).

and abolished either by injection at mandibular foramen on opposite side or mental injection

dle of nail of palpating finger above masticating surfaces of molars, in children and old age lower (See Figure 17); barrel resting on first bicuspid of opposite side. (See Figures 8, 9, 11, 24). Needle is advanced to full length before injecting. If the *lingual nerve*, innervating soft tissues lingually, is to be anesthetized, 0.5 cc. of solution (1-4 of syringe) is discharged when needle has entered the soft tissues half-way. When injecting on the right side, operator stands in front of patient; when on left side, operator stands on right side, his arm placed around patient's head palapting retromolar triangle with left index finger. In either case patient is seated erect, mouth wide open. Quantity of solution 2 cc. (one full syringe).

Figure 15. Dissected specimen showing relative situation of the lingual and mandibualr nerves and the mandibular artery in the pterygo-mandibular space; also absence of danger of puncturing mandibular artery with slow and cautious injection, (Zuckerkandl).

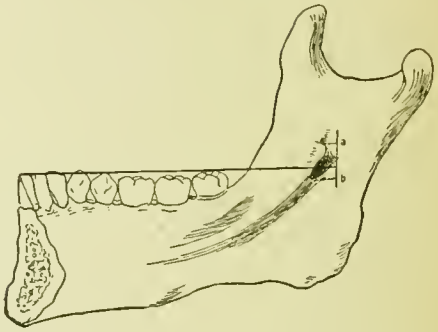

Figure 16. Situation of the mandibular foramen Bünte and Moral).

MANDIBLE—FACIAL SURFACE

(1) *Mental foramen,* located beneath and between the roots of the first and second bicuspids, where *incisor branch* of mandibular nerve, innervating bone and pulps of first bicuspid (sometimes), canine, and incisors, also *mental branch,* innervating skin of chin, skin and mucous membrane of lower lip, and anastomosing branches of inferior dental and mental nerves from the other side are blocked. Palpate foramen on face with tip of left index finger, depressing lip with thumb. Needle in-

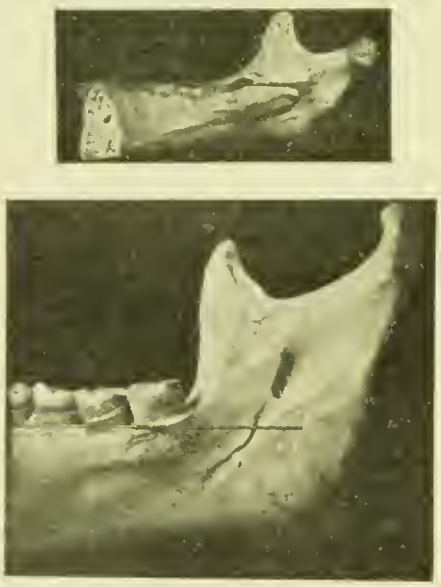

Figure 17, 18. Comparative situation of mandibular foramen in the young child and adult, (Bünte and Moral).

Figure 19. Position of syringe and needle in the mandibular injection.

serted in reflection of mucous membrane between the two bicuspids, and advanced while injecting almost vertically downward (See Figures 6 and 8); since foramen open distally, until the discharging solution is felt under palpating finger-tip. Operator stands behind patient, who is seated erect, mouth half open. Quantity of solution: 1cc. (1-2 syringeful).

(2) *Buccinator nerve,* supplying the buccal mucosa of molars and bicuspids and angle of

mouth with sensory fibers. Needle inserted in second bicuspid region (See Figures 6 and 8), half-way between cervical margin and reflection of mucous membrane, and advanced parallel with masticating surface of molars while continually injecting on bony surface. Injection in cheek opposite second bicuspid indicated if prolonged operation is to be made, to avoid pain in buccinator muscle from prolonged opening of mouth. Operator stands in front of patient, who is seated erect, mouth half open. Quantity of solution: 1 cc. (1-2 syringeful).

(3) *Extra-oral anesthesia of the mandibular nerve,* indicated in cases of extensive infection of the oral cavity and of impossibility to

Figure 20. Position of palpating index finger, right hand, syringe and needle in the mandibular injection.

open the mouth, as in ankylosis and fractures, and first suggested by Pehr Gadd in January, 1913, may prove valuable, though not uniformly successful owing to absence of reliable landmarks. This method, which has been lately again recommended by Klein and Sicher,[34] is indicated in Figure 9, *b*.

The rapidity of establishment of anesthesia following the various forms of injection, and the duration of the anesthesia, greatly depend upon the perfection of the operator's technic and the patient's individual susceptibility. The former can be advantageously enhanced by digital or vibratory massage of the injected tissues when accessible. The depth of the anesthesia should always be tested by a suitable sharp instrument before proceeding to operate.

THE MIDDLE SUPERIOR ALVEOLAR NERVE

In the above table all undue detail has been purposely avoided. The special anatomy of the field involved, an intimate knowledge of which is not only the *sine qua non* of success, but a duty toward the patient, can be studied in any text book on general anatomy, or in text-books on Local Anesthesia, such as Braun's, and Allen's for general, Lederer's and Fischer-Reithmüller's for dental surgery, and in Blum's article on "Conductive Anesthesia.[35] In the last article is also found a *résumé* of the widely diverging opinions of anatomists reagrding the course of the middle alveolar dental branch. In most cases I have been able to anesthetize the three molars and bicuspids together by an ordinary tuberosity injection, which must be due to the fact that the middle branch enters the body of the bone either in the

Figure 21. Method of mandibular injection on the left side.

cribiform area indicated in Figure 10, or in foramina situated anteriorly thereto; in the latter case the middle branch is anesthetized by the depot of solution laid in withdrawing of the needle. If either of the bicuspids, or both, persist in remaining sensitive following tuberosity injection, infiltration facially between the first and second bicuspids, or infraorbital injection for the first bicuspid, will solve the problem. An improvement in the technic so as to afford safe anesthesia simul-

taneously of the posterior, middle and anterior superior alveolar nerves by one injection high up in the pterygo-palatine canal has not as yet been devised, but may not be far from realization.

PRE-OPERATIVE MEDICATION

One feature in anesthesia which has received altogether too scant consideration by the dentist, is pre-operative medication by mild narcotics. The most suitable of these for dental operations are bromural (alpha-brom-isovaleryl-urea), one tablet (equal 0.3 gram) for children, two tablets for adults, to be taken with water from thirty to forty-five minutes before operating, and chloral hydrate, from 0.5 to 1 gram. In cases of great excitement and fear, camphorated validol, 10 drops in a little water; or in extreme cases, morphin 0.02 gram and hyoscin 0.005 gram in aqua destillata 10 cc., from 6 to 8 drops in a tablespoonful of water; or morphin 1-5 grain and scopolamin 1-150 grain, hypodermatically, the dose in alcoholics and especially muscular men to be 1-4 gr. morphin and 1-150 gr. scopolamin. These pre-operative sedative measures apply to general and local anesthesia alike.

Figure 22. Green skull injected with bismuth paste and radiographed, (see also Figures 23 and 24). Note faulty position of the needle, which has missed the pterygo-mandibular space, the internal pyterygoid muscle having been injected instead, (Türkheim).

THERAPEUTIC MEASURES IN COLLAPSE

Any alarming symptoms arising in the course of a local anesthesia are the more easily combated, the more quickly the operator applies suitable antidotes which will also minimize shock. The first few seconds are the most valuable for resuscitation, hence it behooves the operator to be familiar with restorative means and to have them at his elbow. The German law making it a misdemeanor for an operator to administer an anesthetic without having at least a sterile hypodermic syringe and ampules containing strychnin or camphor in oil ready for use, deserves emulation.

Figure 23. Slightly high injection. Note the remarkable diffusion of the bismuth paste even in dead tissue (Türkheim).

If light symptoms of collapse appear, such as pallor, nausea, palpitation, rapid pulse, perspiration, trembling, a decoction of black coffee, fresh aromatic spirits of ammonia, or camphorated validol 8 to 10 drops in a tablespoon-

ful of water, may be advantageously given. The inhalation of amyl nitrite, placing of the patient's head in a recumbent position, heart stimulation, wrapping of the chest in wet cloths, a hypodermic injection of camphor in oil, inhalation of oxygen, and artificial respiration, must be resorted to in proportion to the gravity of the symptoms arising and the degree of effect of the restorative means employed.

Figure 24. Correct injection. Note diffusion of bismuth paste in the pterygo-mandibular space, (Türkheim).

Again, the more quickly these restorative means are applied the milder their nature may be, and the more successfully will shock be warded off.

POSTOPERATIVE TREATMENT

The postoperative care of the patient is not least in importance, if health is to be restored in the shortest possible manner and a perfect anoci sequence is to be obtained. A painless and rapid process of repair is best insured by protecting wounds, as for instance those due to extractions, against external stimuli and irritation of the traumatized tissues, by spraying or tamponing with pure orthtoform or novocain powder, according to Spiess's method, after previous antiseptic dressing with 10 per cent. iodoform or europhen. No inflammation will develop if the reflexes conveyed from the traumatized area by way of the afferent sensory nerves are successfully blocked by anesthesia, and the normal function of the vasomotor nerves is not interfered with. Internal administration of trigemin 0.25 gram per dose, pyramidon 0.3 gram per dose, or aspirin 0.3 gram combined with pyramidon 0.1 gram, will render excellent service in preventing postoperative shock and allaying after-pain.

CONCLUSION

In conclusion, I cannot warn too emphatically against the haphazard and careless use of local anesthesia by unskilled operators, and against blind fanaticism tending to cast aside and even discredit older and equally well-tried methods of anesthetization. An exceptionally intimate familiarity with the immense bulk of medical and dental literature on this subject, both domestic and foreign, has convinced me of the correctness of my former statement that *"No dental operator who is familiar with but one method should consider himself competent in anesthesia, nor can any dental office which offers anesthetic facilities of but one kind be regarded as efficiently equipped."*

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ANOTHER REFORM NEEDED IS THE APPOINTMENT WITHIN OUR HOSPITALS OF AN ADEQUATE NUMBER OF OFFICERS FOR THE SPECIAL ADMINISTRATION OF ANESTHETICS, THE SENIOR OF SUCH OFFICERS BEING A MEMBER OF THE STAFF AND POSSESSING ACADEMIC OR PROFESSIONAL QUALIFICATIONS SIMILAR IN EVERY RESPECT TO THOSE REQUIRED FOR OTHER STAFF APPOINTMENTS AT HIS PARTICULAR HOSPITAL. THIS SPECIAL DEPARTMENT OF PRACTICE SHOULD, IN FACT, BE EXPANDED IN SUCH A WAY THAT EVERY ANESTHETIC ADMINISTERED WITHIN OUR HOSPITALS IS GIVEN BY AN OFFICER APPOINTED FOR SUCH DUTIES. THIS WOULD, OF COURSE, INCREASE THE NUMBER OF JUNIOR HOSPITAL APPOINTMENTS, BUT IT WOULD BE OF GREAT ADVANTAGE, NOT ONLY TO THE PUBLIC, BUT TO THE PROFESSION, TO HAVE A CONSTANT STREAM OF EXPERIENCED ANESTHETISTS ISSUING FROM OUR GREAT CENTERS OF MEDICAL EDUCATION. THE PRESENT REQUIREMENTS OF SURGERY, SO FAR AS THE ADMINISTRATION OF ANESTHETICS IS CONCERNED, ARE OF A TOTALLY DIFFERENT ORDER FROM THOSE WHICH PREVAILED TWENTY OR THIRTY YEARS AGO, AND TO MEET SUCH REQUIREMENTS, THE MODERN ANESTHETIST HAS COME INTO EXISTENCE.

—Sir Frederic W Hewitt.

INTRA- AND EXTRAORAL METHODS OF CONDUCTIVE ANESTHESIA . GENERAL CONSIDERATIONS . PTYREGO-MANDIBULAR, ZYGOMATIC, INFRAORBITAL, MENTAL, INCISIVE, POSTERIOR PALATINE AND MAXILLARY INJECTIONS . INSTRUMENTARIUM . SOLUTIONS AND THEIR REQUIREMENTS . PREPARATION OF PATIENT . APIECTOMY . ANESTHESIA FOR APIECTOMY . FAILURES AND DANGERS . TECHNIC . CASE REPORTS .

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CONDUCTIVE ANESTHESIA is the ideal method of producing anesthesia in and about the oral cavity. The main advantages over the local methods are the following: (1) a comparatively larger area can be anesthetized with one injection; (2) the needle is inserted at a point quite remote from the field of operation, which has its obvious advantages; and (3) the anesthesia, as a rule, is of long duration. Conductive anesthesia is also a method which can be combined with injections into the field of operation to diminish the bleeding, or with general anesthesia to prevent physical as well as psychic schock.

We distinguish two principal modes of conductive anesthesia: the *intraoral* and the *extraoral* methods.

INTRAORAL METHODS OF CONDUCTIVE ANESTHESIA

Intraoral injections will probably always be more popular than the external ones. They enable us to anesthetize the teeth and other areas in the mouth in a perfectly effective manner so that under its influence any dental or minor oral surgical operation may be satisfactorily performed.

The principle in conductive anesthesia is to intercept or block the conductivity of the main nerve-trunk supplying the parts to be obtunded, at a convenient point. There are six convenient places in the oral cavity where conductive anesthesia can be readily induced.

Minute details of these methods have been worked out by practical experience and are of the greatest importance for uniformly good results. The technics thus developed have been proven reliable by thousands of successful injections. It is unnecessary here to enter into a detailed description of the minutiae of these technics, as they can be studied in text and illustrations in various works on local anesthesia. (See: Kurt H. Thoma: Oral Anesthesia; and Fischer-Riethmüller: Local Anesthesia in Dentistry). In this article only a condensed description of the application and results of the different methods will be given.

THE PTERYGO-MANDIBULAR INJECTION

PREPARING THE SITE OF INJECTION.—Dry and clean the mucous membrane with sterile gauze and apply tincture of iodin where the needle is to be inserted.

LANDMARKS.—Palpate the external and internal oblique line, place tip of finger in the depression between the two lines forming the post molar triangle.

INSERTION OF THE NEEDLE.—The point of insertion is on the internal side of the palpating finger tip 1 cm. over the last molar. (Figure 1).

INJECTION OF THE LINGUAL NERVE.—Insert the needle to the depth of 1 cm. and inject 1-2 cc. at the anterior margin of the pterygoid muscle, near the lingual nerve.

INJECTION FOR THE INFERIOR ALVEOLAR NERVE.—Feel the internal oblique line with the point of the needle, push the needle backwards

and slightly outwards, while keeping in close contact with the inner surface of the ramus. When the needle is inserted to the hub, the point extends into the pterygo-mandibular space in which the alveolar nerve enters the mandibular foramen. Inject 1 1-2 to 4 cc. of the analgesic solution. (Figure 2).

SYMPTOMS OF ANESTHESIA.—In a short time, usually about 5 minutes, the patient feels a tingling, hard, stiff or numb sensation on the tip and side of the tongue and that side of the lower lip in which anesthesia has been induced.

ANASTOMOSING AND COMMUNICATING NERVES.—When operating in front of the mouth it should be borne in mind that it may be necessary to block the nerve coming from the other side which anastomoses in the median line. The buccal nerve supplies the gum on the buccal side in the lower molar regions, while at the lower border of the jaw we have to consider communicating branches from the cervical plexus.

DURATION OF ANESTHESIA.—If 1 1-2 to 2 cc. of solution is injected the anesthesia usually

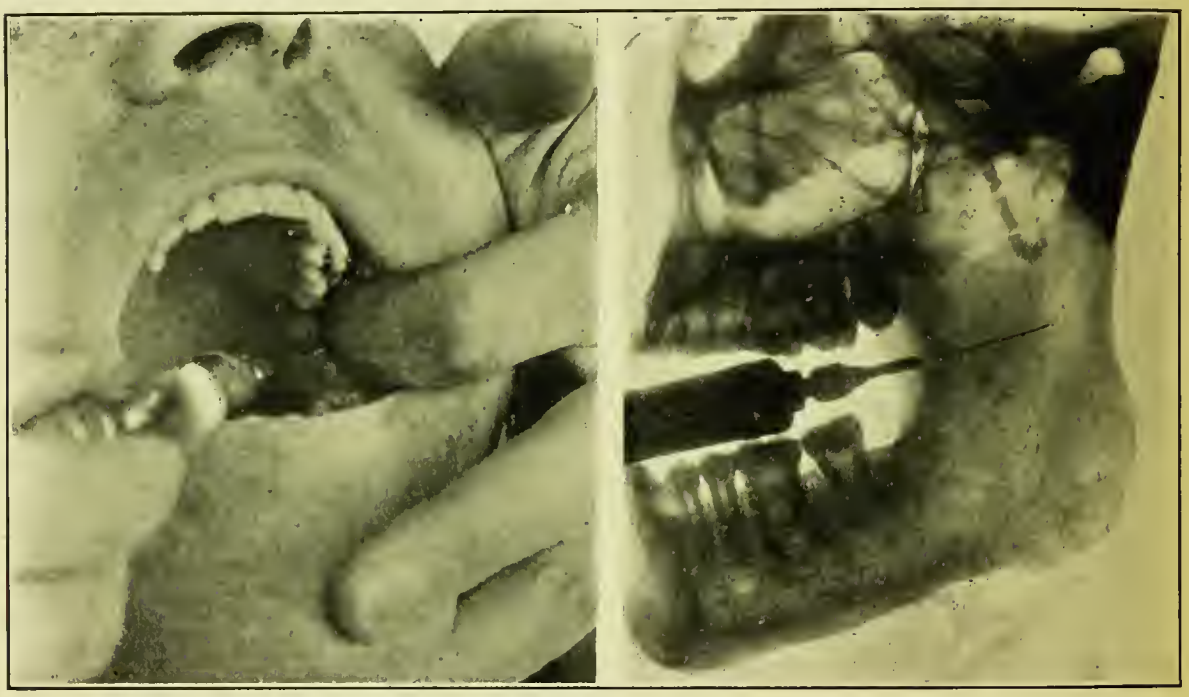


Figure 1, 2. Pterygo-Mandibular injection, intraoral method. Position for left side. (2) Radiograph (positive) showing the position of the needle in the pterygo-mandibular space.

WAITING PERIOD.—The anesthesia takes effect in from 10 to 20 minutes and is at its best in 30 to 40 minutes.

AREAS ANESTHETIZED. — Externally, the lower lip and the region of the corners of the mouth as far back as the mental foramen. Internally, all the lower teeth and the lower jaw of the respective side, the gum on the lingual side and the side of the tongue and the labial part of the gum of the anterior teeth as far as the mental foramen. Also the mucous membrane of the post molar triangle and the gum buccally to the lower wisdom tooth.

lasts from one to one and a half hours; if 4 cc. of solution is injected the anesthesia persists from two to three hours. A second injection may be made during the operation if necessary.

RETURN TO NORMAL.—The anesthesia wears off gradually through absorption of the anesthetic solution.

THE MENTAL INJECTION

PREPARING SITE OF INJECTION.—The lip is retracted and after the mucous membrane has

been cleaned and dried, apply tincture of iodin in the region between the gingival margin and mental foramen.

LANDMARKS.—The mental foramen lies between the two bicuspids and half-way between the gingival and the inferior alveolar border. Place the tip of the palpating finger directly over the mental foramen.

AREA ANESTHETIZED.—This injection is not very satisfactory if used alone. If used on both sides simultaneously an anesthesia of the cuspid and incisor teeth may be secured. If used in conjunction with the mandibular injection on the opposite side it serves to block the anastomosing nerves.

DURATION OF THE ANESTHESIA.—The anesthesia induced by the mental injection usually lasts about an hour.

Figures 3, 4. Mental injection, intraoral method. Position for right side. (4) Radiograph (positive) showing position in needle in the mental foramen.

INJECTION.—Insert the needle in the region of the first bicuspid and push it down and slightly backward along the bone until it is felt under the finger. (Figure 3). Inject 1 cc. of the solution into the mental foramen while applying pressure with the finger tip. (Figure 4).

SYMPTOMS OF ANESTHESIA.—This injection will cause analgesia of the region injected, the bicuspids and numbness of the lip. The tongue and lingual parts, however, are not affected.

WAITING PERIOD.—Anesthesia usually occurs in 10 minutes.

THE ZYGOMATIC INJECTION

PREPARING THE SITE OF INJECTION.—The cheek is retracted with the teeth half closed so as to relax the buccinator muscle. The site of injection is sterilized with tincture of iodin as previously described.

LANDMARKS.—The zygomatic process of the maxilla can be easily palpated and is the landmark for the injection.

INJECTION—Insert the needle opposite the apex of the root of the first molar and proceed backwards, inwards and upwards, keeping in close contact with the zygomatic surface. (Figures 5-6). The solution is distributed over the whole area, that is, the injection begins soon after the needle has been inserted and is continued as the needle is advanced. Inject 2 cc. of the analgesic solution.

Figures 5, 6. Zygomatic injection, intraoral method. Position for right side; and site for inserting needle. (6) Radiograph (positive) showing needle inserted for injection.

SYMPTOMS OF ANESTHESIA.—Symptoms are usually absent from this injection.

WAITING PERIOD.—The anesthesia occurs in 10 minutes.

AREA ANESTHETIZED.—The posterior teeth and corresponding alveolar part of the bone and gum over the molar and bicuspid teeth.

DURATION OF ANESTHESIA. — Anesthesia usually lasts three-quarters of an hour.

THE INFRAORBITAL INJECTION

PREPARING SITE OF INJECTION.—The upper lip is retracted and the mucous membrane is sterilized as previously indicated.

LANDMARKS.—Palpate the inferior border of the orbit. The infraorbital foramen is situated a few millimeters below on the anterior surface of the maxilla and can be easily felt with the finger.

INJECTION.—Place one finger upon the infraorbital foramen, retract the lip and insert the needle in the canine fossa as high in the reflection of the mucous membrane as possible. (Figures 7-8). Advance under periosteum until the needle point is felt under the palpating finger. Inject the solution while applying pressure with the finger to force the solution through the infraorbital foramen, where it reaches the anterior superior alveolar branch.

Inject 1 cc. of the analgesic solution slowly and with even pressure.

SYMPTOMS OF ANESTHESIA.—After a few minutes the patient feels numbness in the upper lip.

WAITING PERIOD.—The anesthesia usually occurs in about 10 minutes.

AREA ANESTHETIZED. — Externally anesthesia of the infraorbital and nasal regions, the upper lip and upper corner of the mouth, results. Internally, the gum over the anterior

Figures 7, 8. Infraorbital injection, intraoral method. Position for right side. (8) Radiograph (positive) showing needle inserted for the injection.

surface of the upper jaw, as well as the anterior teeth and anterior portion of the maxillary bone are obtunded.

ANASTOMOSING AND COMMUNICATING NERVES.—Anastomoses from the opposite side as well as from the posterior branches of the infraorbital nerve, should be kept in mind.

DURATION OF THE ANESTHESIA.—The anesthesia thus induced lasts about three-quarters of an hour.

THE INCISIVE INJECTION

PREPARING THE SITE OF INJECTION.—The anterior part of the palate is dried as already described and iodin is applied over a small area behind the two central incisors.

INJECTION.—The needle is inserted directly behind the incisor teeth and pushed down a short distance until the foramen is reached. About 1-4 cc. is slowly injected into the incisive foramen.

WAITING PERIOD.—The anesthesia occurs almost at once.

AREA ANESTHETIZED.—The only part anesthetized is the anterior one-third of the palate.

DURATION OF ANESTHESIA. — Anesthesia lasts about one hour.

THE POSTERIOR PALATINE INJECTION

PREPARING THE SITE OF INJECTION.—The mouth is opened wide and the palatal part of

the gum in the region of the second and third molar is prepared as already described.

LANDMARKS.—The larger palatine foramen always lies distal to the last molar that has erupted.

INJECTION.—Insert the needle at the gingival margin at a point from whence it can be advanced towards the palatine foramen in a straight line. Inject 1-4 cc. or less. If too much is injected anesthesia of the soft palate results, which is very inconvenient and distressing to the patient.

Figure 9. Method of determining the point of injection for the pterygo-mandibular injection, extraoral method.

AREA ANESTHETIZED.—This injection anesthetizes the lateral half of the posterior two-thirds of the hard palate.

DURATION OF ANESTHESIA.—The anesthesia thus induced lasts about one hour.

EXTRAORAL INJECTIONS

Extraoral injections are indicated in all cases in which intraoral injections cannot be used on account of pathological changes in the parts where the injections should be made. In cases of fracture, bullet wounds, and other injuries which prevent the opening of the mouth, or make manipulation of the lips and cheeks painful, the extraoral injections are especially indicated, as well as in cases of extensive operations, such as excisions of the parts. The extraoral injections are not more difficult than the intraoral ones and it is principally a psychic cause that prevents their more extensive use, because the dentist and even the oral surgeon hesitates to involve parts which are outside the oral cavity and seemingly have nothing to do with the mouth. These methods, however, are more than justified in extensive operations because with them we can not only anesthetize a much larger area, but they permit us to proceed with any operative procedure in a perfectly aseptic manner. They eliminate infection of deeper areas, as aseptic measures are

more readily controlled externally than within the mouth. However, it is important to warn all those operators who are undertaking extraoral injections that these injections are strictly aseptic operations and that infections from extraoral injections are more dangerous because they are much deeper and in close proximity of the brain.

THE EXTRAORAL PTERYGO-MANDIBULAR INJECTION

This injection is made into the same place as the intraoral one, the pterygo-mandibular space. It is indicated whenever the intraoral method cannot be used, as is often the case in fractures of the mandidle and trismus of the muscles of mastication.

PREPARING THE SITE OF INJECTION.—Paint the dry skin with tincture of iodin. It is important to have the skin dry to secure the best action of the iodin. Washing and shaving should be done the day before and in emergency cases it is better to shave dry and refrain from washing. Dehydrants, such as ether or alcohol, are not necessary and only decrease the efficiency of the iodin. After the operation the iodin may be washed off with ether or alcohol. A spray of ethyl chlorid may be applied after the skin has been thoroughly prepared, to make the first insertion of the needle less painful.

LANDMARKS.—A line is drawn from the tragus of the ear to a point marked by the anterior margin of the masseter muscle and the lower border of the mandible. The point where the line is divided in two halves marks the projection of the mandibular foramen upon the skin. (Figure 9). The point of insertion of the needle is at the inner side of the lower border of the mandible, 2 cm. anterior to the angle of the ramus.

Figures 10, 11. Pterygo-Mandibular injection, extraoral method. Showing point for insertion of needle. (11) Radiograph (positive) showing position of needle when inserted.

Postition of the left hand for the injection on the right side: Place the index finger behind and parallel with the posterior border of the ramus, the thumb in the same direction, its tip touching the lower border of the ramus.

Position of the left hand for injection on the left side: The left arm is passed around the patient's head, the thumb is placed behind the posterior border of the ramus, and the index

finger is bent around the angle of the ramus. The head is bent toward the opposite side.

The dismounted needle is inserted at the point described and is pushed upwards and outwards the distance of 2 cm. until the bone is felt. It is then advanced further in a direction parallel with the index finger. (Figures 10-11). After the needle has been inserted about 4 cm. it is in the pterygo-mandibular space, and as the needle is parallel with the nerve, it does not matter if the needle is inserted a little too far. Inject 2 cc. of the analgesic solution.

separately. This can be done in one of two ways: (a) either by withdrawing the needle about 1 cm. and reinserting it in a vertical direction, which brings it further forward, or (b) by inserting the needle about 5 cm., which brings it higher up and near the point of division of the alveolar and lingual nerves.

DURATION OF ANESTHESIA.—The same as for the intraoral method.

CAUSES OF FAILURES.—The advance of the needle may find bony resistance at a depth of 3 cm. This is due to a misdirection of the

Figures 12, 13. Infraorbital injection, extraoral method. Showing point for insertion of needle. (13) Radiograph (positive) showing needle inserted into the infraorbital canal.

SYMPTOMS OF ANESTHESIA.—Numbness of the lip is felt after 5 minutes.

WAITING PERIOD.—Anesthesia takes effect in about 15 minutes.

AREA ANESTHETIZED.—The lower teeth and jaw on the side injected, the lower lip and anterior part of the gum.

ANASTOMOSING AND COMMUNICATING NERVES.—The inferior alveolar nerve on the other side anastomoses in the incisor region and the lip. The lingual nerve supplies the inner aspect of the gum. If anesthesia of this nerve is also required, it must be taken care of

needle point and a striking of the well-marked internal oblique line. The needle may strike bone at once, which may indicate a well-marked protuberance for the attachment of the pterygoid muscle. These mistakes are remedied by changing the direction of the needle.

THE EXTRAORAL INFRAORBITAL METHOD

PREPARING THE SITE OF INJECTION.—The area under the rim of the orbit and above the canine fossa is sterilized with iodin. Ethyl chlorid may be applied by spray to decrease

the pain caused by the insertion of the needle.

LANDMARKS.—The location of the infraorbital foramen has already been described in considering the intraoral method.

INJECTION.—The needle is inserted directly into the infraorbital foramen from the surface of the skin a distance of about 1 1-2 cm. It is important to determine, before mounting the syringe, that the needle has not entered a blood vessel, which would be indicated by the seeping of blood from the needle. 1 1-2 cc. of the analgesic solution are injected with low and even pressure. (Figures 12-13).

WAITING PERIOD.—The anesthesia usually occurs in a very short time.

AREA ANESTHETIZED.—The same as in the intraoral method.

DURATION OF THE ANESTHESIA.—In this method as infiltration of the anesthetic solution through the infraorbital foramen, is not depended on, but the injection is made directly into the foramen, a much quicker and more lasting anesthesia results.

THE EXTRAORAL MAXILLARY INJECTION

Conductive anesthesia of the upper jaw has never been as satisfactory as for the lower jaw, because there is no place where the blocking of the maxillary division can be undertaken successfully from the oral cavity. The intra-oral conductive methods, therefore, have never been able to replace the local or infiltration methods, because the conductive methods required numerous insertions of the needle and these points of injection were not remote enough from the field of operation, to come outside the diseased zone in extensive lesions. While the teeth and adjacent structures may be obtunded and operated on by means of intraoral and infiltration methods in more extensive oral surgery, in the presence of sepsis,

Figure 14. Maxillary injection, extraoral method. Landmarks to find point for inserting the needle. (A) Anterior margin of the masseter muscle.

trismus, fractures, growths and under certain conditions such as war, the extraoral maxillary injection becomes the method of choice.

PREPARING THE SITE OF INJECTION.—The skin in the area of the zygomatic arch is sterilized with iodin.

LANDMARKS.—Palpate the superior border of the zygomatic arch and find the place where it forms a right angle with the superior margin of the orbit. This is called the *zygomatic angle*. From this point draw a verticle line downwards and about 1-2 cm. below the point where this line meets the inferior border of the zygomatic arch, is the site for insertion of the needle. (Figure 14).

INJECTION.—With the teeth in occlusion insert the needle with the syringe mounted. A few drops of the analgesic solution are injected into the skin and under it. The needle is advanced in a vertical direction to the cheek, and at a depth of from 2 to 3 cm. some resistance is noted. Here the needle may strike the maxillary tuberosity. Now if only the molars are to be obtunded, the injection may be made at this point, and this constitutes the extraoral method for the zygomatic injection. If, however, the whole upper jaw is to be anesthetized, the needle is advanced in the same direction, guiding it backward to pass the tuberosity, and accomplish its entrance into the spheno-maxillary fissure. (Figure 15). After a further advance of 2 cm. the needle again meets bony resistance when the point encounters the inferior part of the anterior surface of the sphenoid bone, just below the foramen rotundum. The depth at this place is between 5 and 6 cm. 1 to 2 cc. of the analgesic solution is injected here. (Figure 16). The injection is purposely made below the foramen to avoid the nerves supplying the eye, which are sometimes anesthetized by infiltration.

SYMPTOMS OF ANESTHESIA.—After about 5 minutes the patient feels numbness in the nose, sometimes also in the upper lip, but the symptoms are much less marked than in the use of conductive methods on the lower jaw.

WAITING PERIOD.—Complete anesthesia usually occurs in from 10 to 15 minutes.

Figures 15, 16. Maxillary injection, extraoral method. Showing how needle is inserted. (16) Showing direction of needle on skull. Note zygomatic nerve branches.

Figures 18, 19. Mandibular injection, extraoral method. Showing how needle is inserted. (19) Showing direction of needle on the skull.

AREA ANESTHETIZED.—Practically all the parts supplied by the maxillary division are obtunded; the maxillary bone, the teeth, gum, palate, half of the upper lip, the anterior part of the cheek, the skin of the nose, the antrum and parts of the nasal cavity.

ANASTOMOSING AND COMMUNICATING NERVES.—Branches from the outer side have to be considered and also the facial nerve which partly supplies the skin of the cheek.

Figure 17. Mandibular injection, extraoral method. Landmarks to find point for insertion of needle, (A).

DURATION OF THE ANESTHESIA.—The anesthesia lasts from 2 to 3 hours.

UNDESIRABLE SYMPTOMS.—Anemia in the region of the infraorbital artery which causes circumscribed whiteness in that part of the cheek which is supplied by it. Diffusion of the solution into the orbit is liable to occur, causing occular disturbances of short duration. The oculomotor or abducens nerve may be infiltrated, resulting in double vision, weakness in the upper eyelid, dilation of the pupil, and if some of the accompanying vessels are affected, anemia of the eyelids may also be observed. Occasionally anesthesia of the soft palate causes temporary difficulty in swallowing. All these complications, which are occasionally associated with the extraoral maxillary injection, last from 15 minutes to 2 hours, but are fortunately not of a serious nature, and merely inconvenience the patient for the time being. The patient should be warned, previous to the injection, of the likelihood of such complications and also of the harmless and transient character, so that he will not be frightened by and lose his confidence in the operator on account of their incidence. As this method is restricted in use to anesthesia for operations of a serious and extensive character, the occasional occurences of the indicated complications, is no contraindication to its routine employment, since its advantages far exceed its disadvantages especially in comparison with the hazards of general anesthesia and its inconveniences for such operative procedures in the oral cavity.

THE EXTRAORAL MANDIBULAR INJECTION

Anesthesia of the mandible may be very successfully accomplished by the intra- and extraoral method of injection into the pterygomandibular space. For operations on the ramus, especially its superior portion; but if on account of the existing pathological condition, the pterygo-mandibular injection is contraindicated, we may then resort to the extraoral mandibular method.

PREPARING THE SITE OF INJECTION.—Prepare the region below the zygomatic arch as previously described. Use the ethyl chlorid spray if necessary.

LANDMARKS.—A line drawn from the zygomatic angle to the tragus of the ear, is divided into halves and at the dividing point, just below the inferior border of the zygomatic arch, is the place for the insertion of the needle. (Figure 17).

INJECTION.—Insert the needle and advance it in a slightly upward direction. The needle passes anterior to the neck of the condyle and below the zygomatic arch. A few drops of the analgesic solution may be injected at once.

After advancing to a depth of from 3 to 4 cm. the needle should strike the smooth infra-temporal surface, (Figure 18); now feel your way along for 1 more cm. until you strike the mandibular nerve, when the patient suddenly notices a radiating pain in the region supplied by it, (Figure 19). Inject from 2 to 5 cc. of the analgesic solution.

SYMPTOMS OF ANESTHESIA.—These are the same as in the pterygo-mandibular injection.

WAITING PERIOD.—Ten to twenty minutes usually elapse before anesthesia is complete; the interval depending on the proximity of the injection to the nerve and the amount of solution used.

Figure 20. Instruments for intra- and extraoral methods. Fischer's syringes, holding 2 cc. each, with short and long needles for intraoral injections (left side). Record syringe holding 5 cc. and needles (right side). Alcohol lamp with cup-holder and graduated porcelain cup to prepare solution. The instruments are kept in a jar filled with alcohol. Vial of T novocain-suprarenin tablets.

AREA ANESTHETIZED.—The teeth and bone of the mandible, lower lip, corner of the mouth, lower part of the cheek and temporal region.

ANASTAMOSING AND COMMUNICATING NERVES.—The anastomoses from the opposite side and in some operations branches from the cervical plexus must also be considered.

DURATION OF ANESTHESIA.—The anesthesia thus induced usually lasts from 2 to 3 hours.

INSTRUMENTS FOR INTRAORAL INJECTIONS

A Fischer syringe with a 26 and 42 mm. iridio-platinum needle. One large and one small dissolving porcelain cup; a glass jar filled with absolute alcohol and a stand to hold the instruments; a bottle for Ringer solution and a tray to hold tubes of tablets, reserve needles, etc.

INSTRUMENTS FOR EXTRAORAL INJECTIONS

A Record syringe of 5 cc. capacity; with steel and nickel needles of 8 cm. length and a diameter of 3-4 of a mm.

ANESTHETIC SOLUTIONS FOR BOTH METHODS

The experience of the majority of operators is almost unanimous in prefering Ringer solution for dissolving the anesthetic tablets. The following is the simplest method of preparing the solution:

RINGER SOLUTION TABLETS

Sodium chlorid	0.050 gram
Calcium chlorid	0.004
Potassium chlorid	0.002

Sig: Dissolve 10 tablets in 100 cc. of freshly distilled and sterilized water.

TABLETS.—Use either the T tablets alone or

combine E and F tablets to secure the required novocain-suprarenin percentage solutions. I have on several occasions pointed out that the admixture of suprarenin should be cautiously controlled. The toxic symptoms presenting under novocain anesthesia may, in the majority of instances, be traced to too high a percentage of suprarenin, and in consequence, in my routine work I have materially reduced its percentage admixture in all solutions. The mixture which has been found most successful by the writer has been secured by dissolving one E and one F tablet in 3 1-2 cc. of Ringer solution. The T tablets which are now in the market contain the correct proportionate amounts of the analgesic agent and suprarenin, and if dissolved in 1 cc. of Ringer solution, the following solution is the result:

Novocain	2 per cent.
Suprarenin syn.	0.000,02 to 1 cc.

FOR ABNORMAL CASES.—It is advisable in the presence of cardiac disorders, arteriosclerosis, nephritis, and hysteria, to use 2 F tablets and 1 E tablet dissolved in 7 cc. of Ringer solution. This gives a solution containing:

Novocain	2 per cent.
Suprarenin syn.	0.000,009 to 1 cc.

FOR DEEP ANEMIA.—When deep and prolonged anemia is required by the operative procedure done under local injections, it is advisable to use one E tablet to each cc. of normal salt or Ringer solution. This gives a solution containing:

Novocain	2 per cent.
Suprarenin syn.	0.000,05 to 1 cc.

REQUIREMENTS OF SOLUTIONS PREPARED FROM TABLETS

(1) The solution should be used immediately after it has been prepared.

(2) The solution should not come in contact with anything except the porcelain cup in which it is made and sterilized, and the syringe. It should not be left any longer than absolutely necessary either in the dissolving cup or syringe, as the solution is very sensitive, being affected and chemically changed by air, heat, light and especially by alkalies.

(3) The tablets should not be touched by hands or instruments and the tube should be closed immediately after use with a rubber stopper. The tablets are readily decomposed by air, light and especially by exposure to moisture.

(4) The tablets should be white in color. If the uppermost tablets in the tube are discolored from chemical changes caused by improper handling of the tube, they should be discarded, as their use involves danger.

(5) The solution made from the tablets should be crystal clear. If it shows even a faint pinkish discoloration it must be discarded.

(6) The normal salt or Ringer solution should be freshly prepared from distilled and sterilized water.

THE PREPARATION OF THE PATIENT

When local anesthesia is used for ordinary dental procedures, such as extractions and the preparation of cavities, preanesthetic medication is not usually required except in extremely nervous and hysterical patients. Bromural, (alphabrom-isovaleryl-urea) is an excellent sedative for this purpose. One tablet given to children, two to adults, thirty minutes before the operation, in water, will quiet apprehensive and nervous patients, so that the injection and operation may be performed without any trouble. For extraoral injections preoperative medication is always indicated. Bromural is somtimes sufficient, but for extensive operations morphin 1-6 to 1-3 gr. (0.01 to 0.02) should be administered. The narcotic effect of the morphin robs the operating room of its horrors and makes the patient indifferent to the instrumentation and operative manipulation which are always more or less feared or resented.

THE SURGICAL TREATMENT OF CHRONIC ALVEOLAR ABSCESS UNDER LOCAL ANESTHESIA

ETIOLOGY.—There are two processes which lead to the formation of chronic alveolar abscess; (a) the destructive process that starts as an acute periodontitis, forming an acute abscess and terminates in the chronic condition; (b) and the process of formation of inflammatory new-growth, stimulated by the irritation and infection from imperfect root canal

work, (which accounts for the larger number of chronic abscess) and occasionally in association with pyorrhoea alveolaris.

VARIETIES.—Clinically we distinguish two types; the one with a sinus leading into the oral cavity or to the face; the other—a blind abscess —which has no outlet to the mouth or face, and which is not usually recognized except by radiographic diagnosis. If the exudates of the suppuration are discharged through a sinus, antrum infection, stomatitis, tonsillitis, pharyngitis, gastric and intestinal infections such as collitis and appendicitis, may result.

Figure 21. Microphotograph of a section through a lateral incisor root with chronic abscess. Note the lateral location of the apical foramen. Necrossed part of the root, light area (A) is seen; and a part of the inflamed pulp, which was not removed from the root-canal, (B).

If there is no outlet the exudates under pressure enter the lymph or capillary systems and are frequently the cause of malaise, infectuous athritis, endocarditis, toxhemia, nephritis and gastric or duodenal ulcer.

HISTOLOGICAL-PATHOLOGY. — Alveolar abscesses show under the microscope as more or less well-defined masses of granulation tissue. Sometimes a fibrous periferal layer extends from the peridontal membrane, in the inside of which is to be seen the typical picture of chronic inflammation: namely, a large amount of lymphocytes, plasma cells and inflammatory granulation tissue. This is of a very vascular nature. The infection is more or less circumscribed by the fibrous tissue surrounding it and preventing involvement of an extensive localized area, but absorption of toxic material and bacteria takes place just the same, and systematic complications usually results. As a rule a small amount of pulp tissue remaining in the apical foramen from which the proliferation started, still presents. (Figure 21). This is especially well shown in the accompanying microphotograph, which also shows a necrosed condition of the apex of the root. It is evident that such a condition can only be cured by surgical methods.

APIECTOMY

GENERAL CONSIDERATIONS. — Apiectomy, consisting of root amputation and extirpation of the imflammatory granulation tissue, may be easily performed on all the anterior teeth in the upper as well as the lower jaw. The molars are more difficult to operate on for obvious reasons. However, apiectomy can be performed on these teeth, especially on the six-year molars. The operation is indicated in cases of chronic alveolar abscesses, instead of extraction. It is the only safe method of treating the tooth if the root is necrosed at the apex, and if the apical peridontal membrane is destroyed. Apiectomy is also indicated for roots which can only be treated and filled to a certain distance and for roots which have been perforated at the apical part by root canal instruments. Provided that the root and bone is strong enough, the technic is available on teeth that carry crowns and bridges.

TREATMENT OF THE ROOT CANAL.—The root canal should be rendered aseptic by the application of tricresol, formaldehyde or by ionic medication. It should be filled by the *rosin-chloroform-guttapercha method*, which has advantage of making the root-canal filling adhere firmly to the root-canal. The filling is condensed so that it adapts itself to the walls. Any filling or crowning of the tooth is to be performed before the operation so as not to disturb the healing process. (Figures 28-29).

PREPARING THE SITE OF OPERATION.—The mouth should be thoroughly cleansed and

sprayed with an antiseptic solution and the mucous membrane cleansed and dried in the area of the contemplated operation.

ANESTHESIA FOR APIECTOMY

Local anesthesia is the method of choice for apiectomy. Novocain-suprarenin suffices for any required operative procedure, and permits the co-operation of the patient, which is a decided advantage. The percentage of suprarenin shoud not be too high, because at the end of the operation it is necessary to stimulate bleeding in order to fill in the bone wound with a clot for healing purposes. One T to 1 cc. or

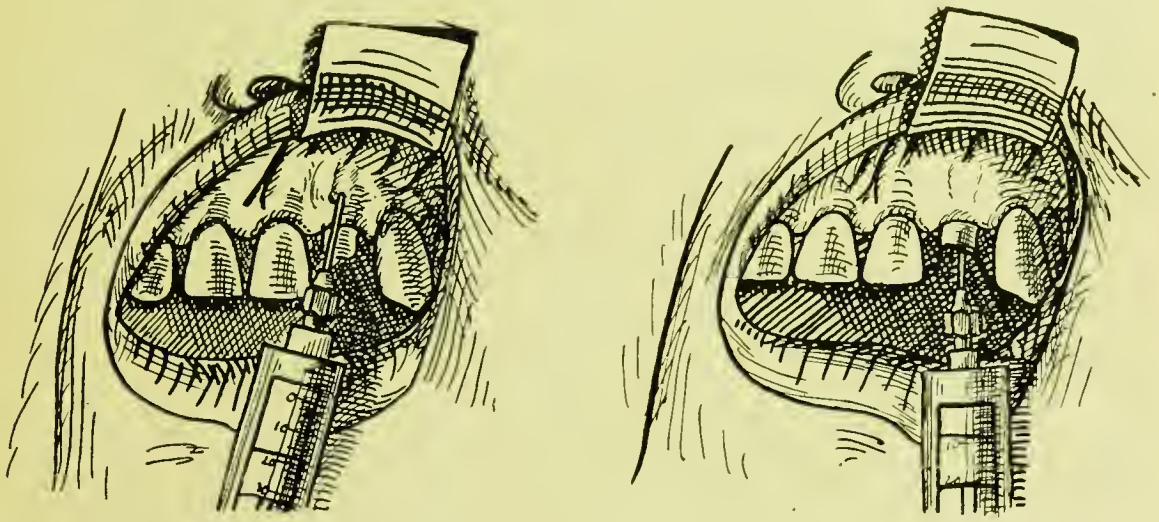


Figure 22 (a-b). Infiltration for apiectomy. (a) Labial injection; (b) palatal injection.

one E and one F tablet combined with 3 1-2 cc. of Ringer solution gives the desired percentage solutions for effective results. Both the outer and inner sides of the alveolar process must be obtunded.

RADIOGRAPHY.—A radiograph may be taken either before the operation or during the waiting period for the anesthetic to take its full effect. An X-ray picture is essential to ascertain the extent of the pathological process and also to determine the extent of the root-canal filling.

PREPARATION FOR THE OPERATION.—The operation should be performed with strict regard to the principles of aseptic surgery. The selected instruments should be sterilized by boiling, and put in order on a sterile table, covered with a terile towel, until they are used.

The patient and operator should be covered with sterile gowns, and the patient's head swathed in a sterile towel, except for the eyes, nose and mouth. The operator should preferably use rubber gloves.

OPERATION.—The saliva ejector is put in place and the lip is retracted with a lip retractor. One piece of sterile gauze is placed on either side of the area of operation so as to avoid contamination of the saliva. The mucous membrane is dried with sterile gauze and painted with 3½ per cent. iodin or aqueous solution of iodin.

INCISION.—With the flap knife a U shaped incision is made as shown in Figure 22. The periosteum and gum are lifted from the bone with the sharp perosteal elevator. A suitable gum retractor is inserted and sterile gauze sponges used to remove the blood.

AMPUTATION OF THE ROOT.—The alveolar process is now visible, if it has not been destroyed by the pathological process and replaced with granulation tissue. A good sized opening is cut with the chisel and mallet or with the aid of the burr, so as to get a clear view of the apex of the root. The apex is resected with a fissure burr to a point not further down than the extent of the root canal filling and as far toward the cervical portion

of the tooth as is necessary to remove all parts which are gangrenous. The resected apex is removed with a suitable elevator. (Figure 23).

CURETTING OF THE ABSCESS CAVITY.—The most important step of the operative procedure is the removal of the inflammatory granulation tissue and the curetting of the alveolar process with a round burr, until all the granulation and diseased bone has been removed and healthy bone presents on all sides. (Figure 24).

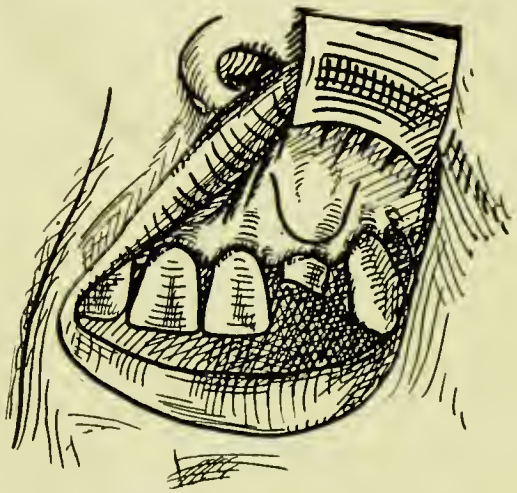


Figure 22. Apiectomy, incision

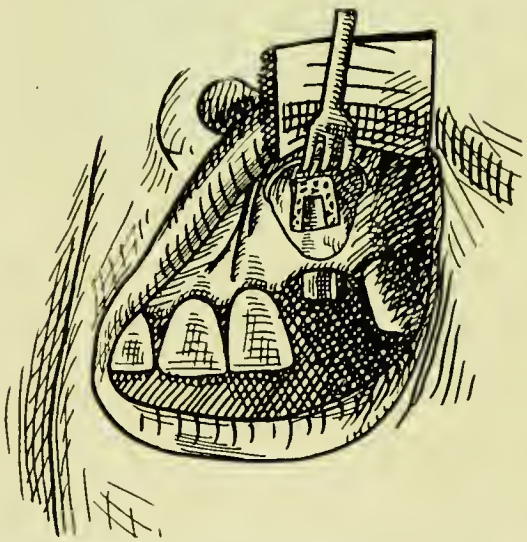


Figure 24. Apiectomy, the root has been amputated and all diseased bone removed.

TREATMENT OF THE WOUND.—All sharp points are carefully removed with the burr and the margins of the alveolar process are rendered smooth. It is not advisable to shape the distal part of the tooth like the end of a root as this decreases the amount of attachment with the bone and tends to loosen the tooth. Personally I prefer leaving a round, clean cavity without anything projecting into it. This cavity is washed out with normal

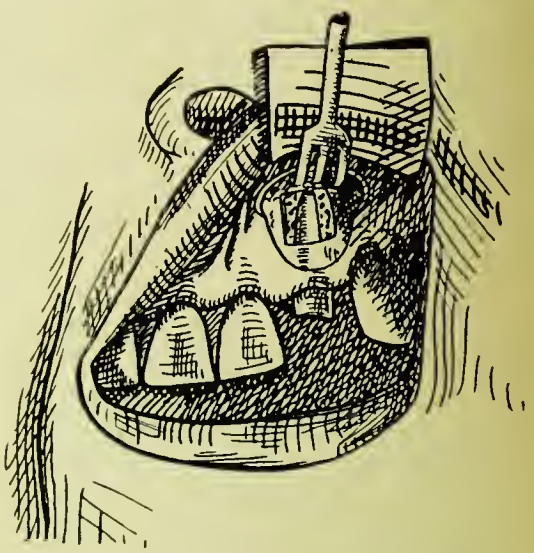


Figure 23. Apiectomy, gum-flap retracted and alveolar process removed to expose the end of the root.

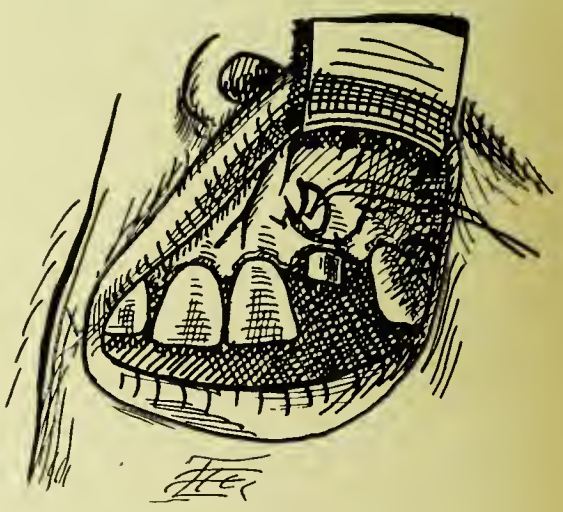
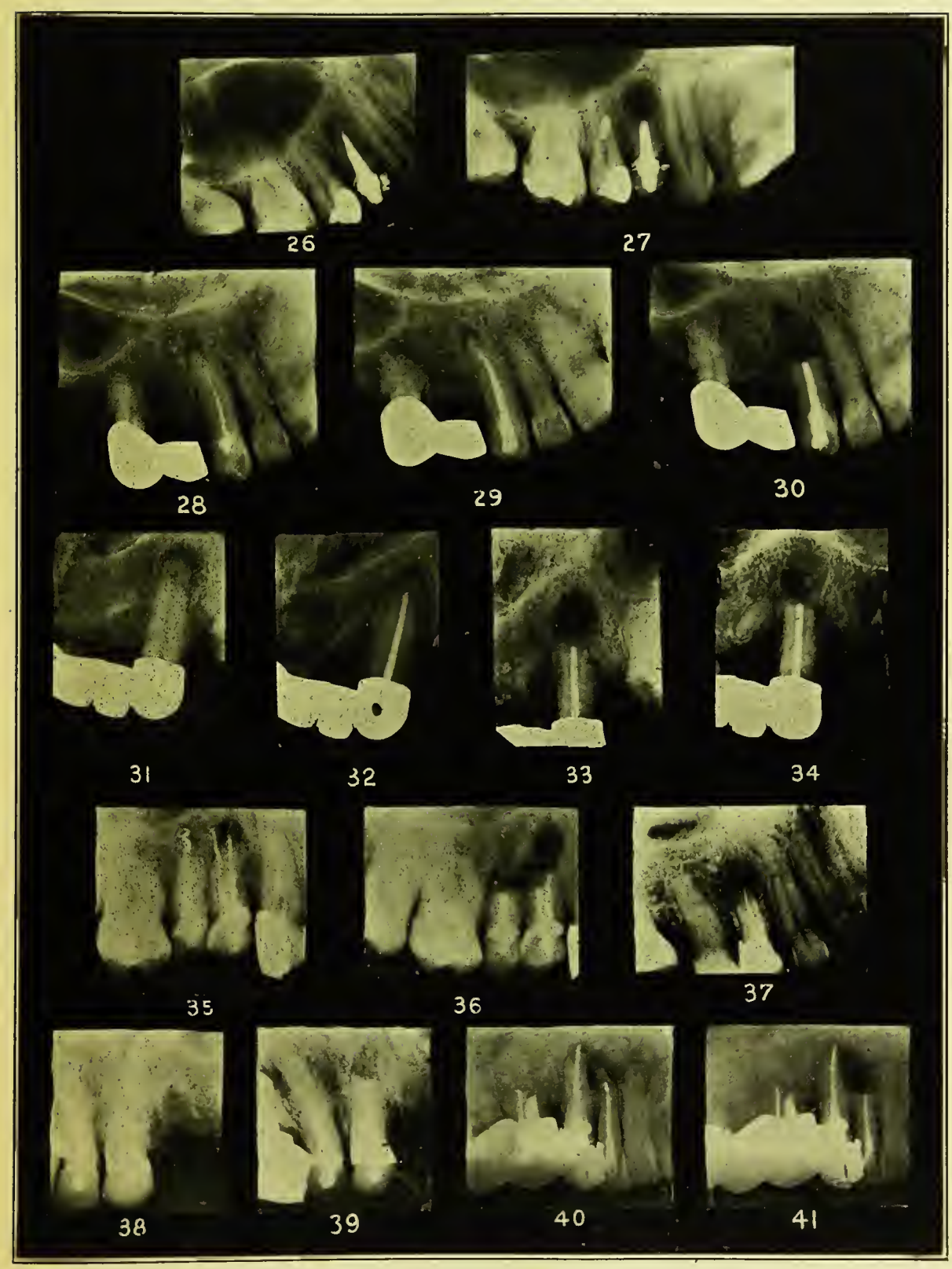


Figure 25. Apiectomy, closing of wound.



Figures 26 to 41. Radiographs (negative) of Case Reports.

salt solution to remove all debris, after which it is sponged dry and sterilized with 3½ per cent. iodin or aqueous solution of iodin. The excess of the antiseptic should be carefully removed by sponging and bleeding, then stimulated to fill the cavity with a fresh clot. When the cavity has been filled, the periosteal and gum flap is drawn over the opening and sewn back into place with several usually 3, horsehair sutures. (Figure 25).

HEALING.—The healing occurs by organization of the blood clot with the later formation of bone, as is shown in some of the radiographs illustrating specific cases. (Figure 37). If proper aseptic precautions and care have been taken, a good union is obtained in a short time. The stitches are removed after three days, and if horse-hair sutures have been used, they cause little or no discomfort to the patient while in position. From my personal experience and results, I can heartily endorse the technic of immediate closing the operative wound to secure healing by first intention and to avoid reinfection from saliva. Exactly the same technic is used by the ear specialists in the radical mastoid operation with the best possible results. The blood-clot method of restoration also gives the best cosmetic effect as the tendency is for the cavity to become filled with new bone and not to leave an unsightly depression or a loose tooth. The patient should be warned, however, that the face will swell up somewhat for a few days after the operation as a result of the mechanical injury of the operative procedure, and for the relief of this postoperative symptom dry heat may be effectively applied. In three to four days the face will assume its normal contour, and except in the occurrence of reinfection, after-pain is negligible.

FAILURES AND DANGERS

In operating for the radical cure of alveolar abscess it is important to remember certain anatomical points, especially that in the upper jaw of the antrum, and in the lower jaw the mental foramen may be accidentally invaded. If the operation is performed with rigid asepsis such complications as the invasion of the antrum or mental foramen will involve no imperiling dangers. Failures in securing proper results may occur either because the granulation tissue has not been thoroughly removed, because a neighboring tooth may be involved, because the root-canal has not been properly sterilized, or because the root may be discolored and necrotic almost to the cervical margin. The last two reasons are the most important ones and always cause reinfection, which can only be eliminated and cured by extraction. Out of 61 consecutive cases in my personal experience, I have to record two failures due to these causes, and I make it a rule now not to operate on teeth, the root canals of which have not previously been sterilized and filled.

CASE REPORTS

CASE 1: Patient had a chronic abscess with sinus on the left upper second biscupid, which was treated by root-canal medication for several weeks, without result. Figure 26 shows the radiograph taken before the operation. Figure 27 is a radiograph taken 5 days after the operation when the wound had healed and the sinus closed.

CASE 2: Patient, Mrs. W., suffered from acute infectuous arthritis, especially manifested in her fingers and toes. She was referred to me by an orthopedic surgeon. Possible foci had been searched for by various specialists with negative results except in the mouth. Radiographs revealed chronic, blind abscesses on the left lower bicuspid and left upper cuspid, Figure 28. I extracted the lower bicuspid and operated on the upper cuspid after the root-canal had been properly sterilized and filled, Figure 29. Compare the root filling the two radiographs. Figure 30 shows the same case after apiectomy on the cuspid. The patient reported after six weeks greatly improved, the acute arthritic symptoms having entirely disappeared.

CASE 3: The patient, Mrs. H., had a blind abscess on her right upper cuspid. The tooth served as an abutment for a cuspid to cuspid bridge which was well constructed, but the tooth had become devitalized for some reason or other, resulting in a blind alveolar abscess, Figure 31. I made an opening in the back of the crown and sterilized the root-canal and tooth properly, and later filled the root-canal, Figure 32. Apiectomy was performed the next day, Figure 33. The stitches were removed after three days, when the wound had healed by first intention. Figure 34 shows the same case after eight months, when the cavity was almost healed by proliferated bone.

CASE 4: The patient, Mr. R., came to me with a history of toxhemia which manifested itself principally in the morning by an intoxicated feeling in the head. His ability to think was greatly decreased and he suffered from time to time from rheumatism in his feet. Radiographs showed abscesses on the upper right incisor, upper left cuspid, first bicuspid and second bicuspid. Apiectomy was performed on the lateral incisor. The cuspid and two bicuspids were thoroughly cleaned and treated with tricresol formaldehyde, and after the dressings remained sweet, I used ionic medication. Root canals were filled, but the points projected through the apical foramen. During treatment

the patient improved greatly and at the end felt perfectly clear as far as his head was concerned, and explained that he could now smoke like a chimney, whereas previously one cigar made him ill. Figure 35. After 8 months he returned saying that two weeks previously his old trouble had recurred. Radiographs showed about the same condition as after treatment, the cuspid was fairly good, the first bicuspids had large areas of increased density. I amputated the roots of both the bicuspids and extirpated the abscesses, Figure 36, and when I saw the patient two days later, he reported that the operation had produced an almost immediate change in his condition.

CASE 5: The patient suffered from a large abscess on the left upper first bicuspid. Figure 37 is a radiograph taken four weeks after the operation and shows the healing process. Small bridges of bone are to be seen growing into and filling the cavity.

CASE 6: Patient, Mrs. C., suffered from general malaise. Figure 38 shows an abscess on the upper cuspid. Figure 39 shows a radiograph taken 5 months after the operation. The abscess cavity is filled with new bone.

CASE 7: Patient referred to me with the history of a broken root-canal instrument in the apical part of the root-canal of the lower lateral incisor. The radiograph, Figure 40, shows the abscess caused by the condition. The distal part of the root is bent and this probably caused the instrument to break. The part of the root containing the instrument was amputated, the abscess cavity thoroughly curetted and sewed up to heal by first intention, Figure 41.

CASE 8: Miss M., patient at the Robert Bent Brigham Hospital, suffered from a chronic abscess of the upper incisor. Figure 42 shows a radiograph after the root-canal work had been completed. Figure 43 is a radiograph taken after the lapse of six months, with obliteration of the cavity.

CASE 9: Patient, Miss B., aged 19 years, suffered from chronic alveolar abscesses on the upper lateral and central incisors. Both were connected with the oral cavity by sinuses and had discharged for several years. Antiseptic treatment from the root canals for 8 weeks gave no appreciable result. The patient was referred to me for apiectomy. I operated on both teeth at once. Figure 44 shows the results immediately after operation, Figure 45 the healing process two months later and Figure 46 the conditions presenting 10 months after operation, in which it may be noted that the density of the bone over the operated teeth is the same as that over the lateral and central incisor on the other side.

Figures 42 to 46. Radiographs (negative) of Case Reports.

AFTER-PAIN IN ITS RELATION TO GENERAL AND LOCAL ANESTHESIA . GENERAL CONSIDERATIONS . TRAUMA AND FOREIGN SUBSTANCES . THE INFLUENCE OF ACCESSORY DRUGS . PERSONAL RESEARCHES IN THE CONTROL OF AFTER-PAIN . VITAL FACTORS IN THE PRODUCTION OF ENDURING ANESTHESIA . AVOIDING COMPLICATIONS IN THE USE OF QUININ-UREA HYDROCHLORID . OPERATIVE GENTLENESS . BIBLIOGRAPHY .

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BY AFTER-PAIN in the sense of this title is understood the unpleasant effects incident to and following an operation. The degree of discomfort required to warrant the designation *pain* is a very varying quantity. The interpretation of the individual patient is the deciding factor and consequently the testimony is subject to endless variation. The patient's own testimony varies. A patient may complain of pain a few hours after the operation, while after a week he may no longer recall his experience as painful, but will attribute his discomfort to the apprehension of possibilities of wound complication. After a week the joy of the riddance from his truss, for instance, may minimize the suffering he endured following the operation.

The estimation of *after-pain* in the abstract is possible only after observing many operations on all sorts of people. One gradually comes to summate his observations into general averages for certain operations. For instance, pile ligations will be followed by greater pain than an operation for hernia.

The personal equation of the observer is a powerful factor. It was once my privilege to hear a noted surgeon say that following his technic for hernia operations after-pain was inconsequential and, from the same platform, a former patient of his, also a surgeon of note, make a real oratorical effort descriptive of real pain suffered following the operation for hernia.

In making an estimate of the *after-pain* a patient suffers, I believe that an intelligent nurse is a better judge than either patient or surgeon. Permit her to observe several hundred patients and she will come pretty near estimating correctly the degree of *actual after-pain* suffered and more correctly estimate the merits of various technics in lessening it than will the surgeon himself.

The only way the surgeon may obtain information, if he does not believe what is told him, is to experiment on himself. In some procedures this method is very valuable. In the determination of the pain produced by and incident to the use of the local anesthetic self-experimentation is easily available. Even in the study of the pain following an incision, its severity and duration, may be determined in this way if the experimentor is not fastidious.

Taken on the whole the problem of *after-pain* has not been taken seriously by the profession. There is but little in the scant literature bearing on this subject and aside from a very few papers the statements are made without much thought and without a sound basis of fact. It is desirable that this problem receive a more careful study, for until a patient may be relieved of his complaint, not only without danger, but also without pain, both during and after the operation, can we claim to be approaching the ideal in surgical technic.

The *after-pain*, we may say, begins after the operation. In considering this problem as it relates to the use of local anesthetics we must include the pain produced by the use of the anesthetic, the prick of the needle, the indura-

tion produced by the anesthetic and the pain of the operative procedure along with the post-operative discomfort. In general anesthesia the unpleasantness of the act of inhalation, the pharyngitis, the tracheal irritation, perchance the pneumonia, and the nausea must be charged along with the wound pain when we make our estimate of the pain of an operation. Even this broad view is arbitrarily narrow and has its justifications in the fact that this comprises all that is physically tangible. To be comprehensive, it would be necessary to to include the psychic states of the patient, both before and following the operation.

Having called attention to the broader phases of the problem, it will be well to centralize the inquiry upon the main phase of the problem; the pain present after the patient recovers from his anesthesia, be that general or local.

In general anesthesia the return of consciousness is dependent upon the kind and amount of anesthetic used. With nitrous oxid consciousness returns at once. With ether several hours may elapse. When local anesthesia has been used return of sensation takes place in a wide range of time which may be broadly placed at from fifteen minutes to fifteen days.

Obviously then in determining the after-phenomena of which he must take cognizance, much depends upon the extent to which the reparative processes have progressed before pain sensations again react on consciousness.

It is necessary before taking up time relations to determine as nearly as possible the factors which produce pain, how long they act, and which factors may modify them. These may be considered under several subheads.

PAINS DUE TO THE TRAUMA OF THE OPERATION

The severance of nerve fibers and nerve endings are the factors which cause pain. Why this causes pain we do not know. Obviously it serves to warn the animal against impending injury. While this may be a satisfactory answer as to the *why*, it does not aid in determining the *how*. All that can be said is that the severance of nerves is followed by pain and that, generally speaking, those regions most abundantly supplied by nerves are most painful when operated on.

The interesting question may be raised as to the purposive action of continued pain. Momentary pain would be sufficient to warn against impending danger. For instance, the sting of a bumble bee, judiciously placed, is sufficient to propel the small boy beyond danger. The continuance of the pain would seem to have no purpose. That *after-pain* is associated with the essential processes of repair does not seem likely. Sensory and trophic nerves are separate. Healing following the use of quinin may be well advanced before sensation returns. It seems evident therefore that we are as yet unable to clearly state our minor premise. Nevertheless, we may assume that continued pain provides the necessary rest for the injured part in order that the most favorable conditions for repair may be assured. The abstract question may present itself if it were possible to prevent *after-pain* whether or not we would be defeating a necessary provision of nature.

That operative trauma is followed by pain is evident. The duration of pain following simple trauma is not great. Several hours probably covers the duration of pain following the simple severance of tissues when not followed by complicating factors. The factors which complicate here are those necessarily due to the manipulations of the operations and the mechanical factors which must enter in order to produce the result we desire. The ligation of vessels including nerve filaments, and the suturing of nerve-bearing tissues are the chief factors which increase the *after-pain* beyond that produced by the wound itself. Pinching of nerve-bearing tissues, ligation *en masse*, the inclusion of avoidable nerves in ligatures and sutures are the avoidable causes of *after-pain*.

FOREIGN SUBSTANCES INTRODUCED INTO THE WOUND

In addition to the mechanical factors just enumerated, increase of after-pain may be caused by the presence of chemicals in the wound. Iodin and chrome salts in the cat-gut

are productive of tissue reaction as compared with silver wire, silk, worm-gut, or celluloid linen. Bactericidal agents act in a like manner. The old iodoform-glycerin mixture is capable of producing the most atrocious *after-pain*. A study of the effect of these various drugs on the tissues reveals that the reaction of the tissues to them is indistinguishable from the reaction of inflammation. Perhaps the old term *aseptic inflammation* would be descriptive of the reaction. Iodoform-glycerin or formalin-glycerin for instance produces an abundant exudate into the tissues which is quite as painful as a like degree of swelling produced by bacterial infection. The degree of exudate and not the numerical presence of extraneous cells is the determining factor.

After-pain therefore is less dependent upon the size and site of the wound than upon the manner of doing the essential and committing the innumerable sins against gentle technic. Each of these may be complicated by slight or severe infections which may or may not produce gross wound disturbance.

The prevention of *after-pain* is primarily a study in repair, and should be preceded by a comprehensive study of wound healing and of the reaction of the tissues to injury.

Infections, slight in character, which are subdued by the reactive factors in the body add materially to the *after-pain*. These factors may be overlooked when they play their roll in tissues other than the skin. Wounds that retain deep sensitiveness are indicative of reactive disturbances and are apt to heal imperfectly. When such processes involve the abdominal wall hernias are more apt to follow than after uncomplicated wounds.

The foregoing, briefly presented, are the factors, which the student of local anesthesia is called upon to combat with his drugs. That his results cannot be uniform unless the technic of his operations is uniform goes without saying. The comparison of results of individual operators is difficult and for one operator to copy the methods of another for the prevention of after-pain is futile unless he also copies his general operative technic.

CONTROL OF AFTER-PAIN BY ACCESSORY DRUGS

In calculating *after-pain* other complicating factors are often introduced. Chief of these are the drugs employed accessory to the anesthetic, whether the anesthetic be local or general. It is the practice quite generally to employ morphin or some of its cogeners before the administration of an anesthetic. Obviously these modify the degree of *after-pain*.

In a paper before the Western Surgical Association Dec. 19, 1914, I attempted to represent the duration of pain graphically as follows: Assume that *after-pain* following a given operation will last ten hours. Say the patient regains consciousness after an hour. He has nine hours of pain yet before him. If he has received morphin before the beginning of the anesthetic this will modify postoperative discomfort. Say the effect of morphin lasts six hours. He then has only four of the ten unmitigated by the influence of drugs, to suffer *after-pain*. With local anesthesia the same factors enter in. The effect of the anesthetic will last two hours (novocain-epinephrin). After the effect of the local anesthetic has passed off he has but 8 to 10 of the after-pain remaining. If he has received morphin before the local anesthetic was used, its obtunding effect will be active some hours following the disappearance of the effect of the local anesthetic. The use of the novocain cannot be regarded as of much importance because of the brief duration of its action. The use of morphin in conjunction with it, as is usually done, is of more importance than the use of the local anesthetic itself. The problem therefore of how to employ the local anesthetic in such a way as to mitigate the *after-pain* is of less importance than the duration of the action of the drug. When no morphin is used and the patient is operated on under general anesthesia, can the *after-pain* be controlled by the use of local anesthesia? It can for the duration of the local anesthesia only. If, after a pile operation under ether, novocain is injected, the patient will be free from *after-pain* for about two hours following the injection of the local anesthetic. If he awakens from the ether before this time and is not too much preoccupied by the ataxia of his diaphragm, this freedom from local pain during these two hours may be a factor of some importance, in his postoperative comfort.

Obviously on the average the margin is not

a wide one. The problem has recently been complicated by the supposition that tissue severed while under local anesthesia is subject to less after-pain than when not so injected. To present this problem specifically, if two incisions an inch long are made, the problem to be determined is, which will be the more painful after three hours. In the unanesthetized skin there is a momentary sharp pain when the incision is made. This is followed by burning. The incision made under local anesthesia is painless. At the end of two hours burning begins. This increases in intensity and far exceeds that in the wound made without any anesthesia after the lapse of say three hours.

The reason for this is that in the latter case the trauma of the anesthetic itself must be added to that produced by the knife. This reaction of the tissue to the anesthetic has received but little attention. Obviously if any substance is capable of interfering with the conduction of nerve impulses some changes of a physical or chemical nature must be produced in the tissue. The statement is quite generally made that some local anesthetics are not accompanied by tissue reaction. This is not true. There is no local anesthetic that can be used that does not produce injury to the tissue. This must always be added to the injury produced by the operation itself.

PERSONAL RESEARCHES IN THE CONTROL OF AFTER-PAIN

There is so little in the literature bearing on this subject that I venture to present some of my own researches on this problem.

Various methods are open for investigation. Animals may be employed. The drug under investigation may be studied by its action on the vessels, or the tissues may be removed and their histology and histo-chemistry studied. The same points may be observed in the human subject during the course of an operation. The effect of the drug is noted while it is being introduced. At the termination of the operation a bit of tissue from the edge of the wound may be removed for histologic study. The investigator may observe these phases on his own person.

I have employed all of these methods of investigation for most of the drugs employed in local anesthesia, and also those various drugs combined with other chemicals employed to enhance or modify the action of the principal drug. I shall here detail only observations made with novocain and quinin when used alone and when combined with substances recently recommended to increase or prolong their action.

The first point that will impress the self-experimentalist is obviously the prick of the needle. A fine bright needle with a sharp point carefully introduced produces only a slight burning pain. If no injection is made this injury from the needle alone is scarcely perceived. If a large needle, particularly one with a rusted or obtuse point, is used the pain may be noteworthy and the soreness resulting may remain for days. This is the reason why in major work under local anesthesia it is my practice to run the skin infiltration line with a small needle and make the punctures for the deep infiltration through the primary line. I should want to escape the primary puncture from the big needle and I am sure the patient would if he knew the difference.

To the mechanical effect of the needle must be added the mechanical effect of the fluid. That is to say, if the fluid is injected forcibly into the tissues there is not time for the fluid to diffuse and the tissue fibers are torn apart. In the experiments to be detailed this factor was eliminated.

Pinching up the skin until it is anemic (Figure 1) lessens the sensitiveness of the skin to the initial prick of the needle and lessens the slight burning incident to the first injection of the fluid. This point in the technic may seem trivial, but frequently all the patient recalls of the pain is that produced by the first prick.

Experiments with novocain were made with this drug alone, combined with adrenalin, and combined with various other chemicals to be detailed below. I present herewith (Figure 2) the plan on which these comparative experiments were conducted. I do this for the purpose of impressing upon the reader that much loose conversation has been emitted relative to the duration of local anesthetics and their power to control after-pain. Novocain in 1 per cent. solution in plain water (1-*Figure* 2)

or in normal salt solution was attended by marked capillary dilatation with mild smarting during introduction of the drug. In a few seconds anesthesia is complete while capillary dilatation continues. In about 15 minutes the anesthesia rapidly disappears while the capillary flush continues. This likewise soon disappears, however, and a period of hyperesthesia supervenes together with slight deep tenderness. After 2 to 4 hours there are no longer obvious changes. These phenomena are constant for the individual but seem to vary for different individuals. This is true for the degree of capillary dilatation and for the duration of anesthesia. The maximum duration for novocain alone, in all individuals studied, is 30 minutes, the man less than 20 minutes.

When epinephrin is added the entire picture changes. Instead of preliminary flushing the parts become anemic at once (*2-Figure 2*) and anesthesia is simultaneous with the blanching, provided the injection is made endermically. In a few minutes, usually about 15, the skin becomes papillated from the contraction of the erectores pillorum, the co-called *gooseskin* (*3, 4 and 5-Figure 2*). This is a very striking manifestation of the power of epinephrin to cause the contraction of non-striated muscle fibers. When the injection is made subdermically about 5 to 15 minutes are required for complete anesthesia to set in. Moderate hyperesthesia about the injected area begins after half an hour. After an hour and a half anesthesia begins to lessen, and after three hours is replaced by hyperesthesia to

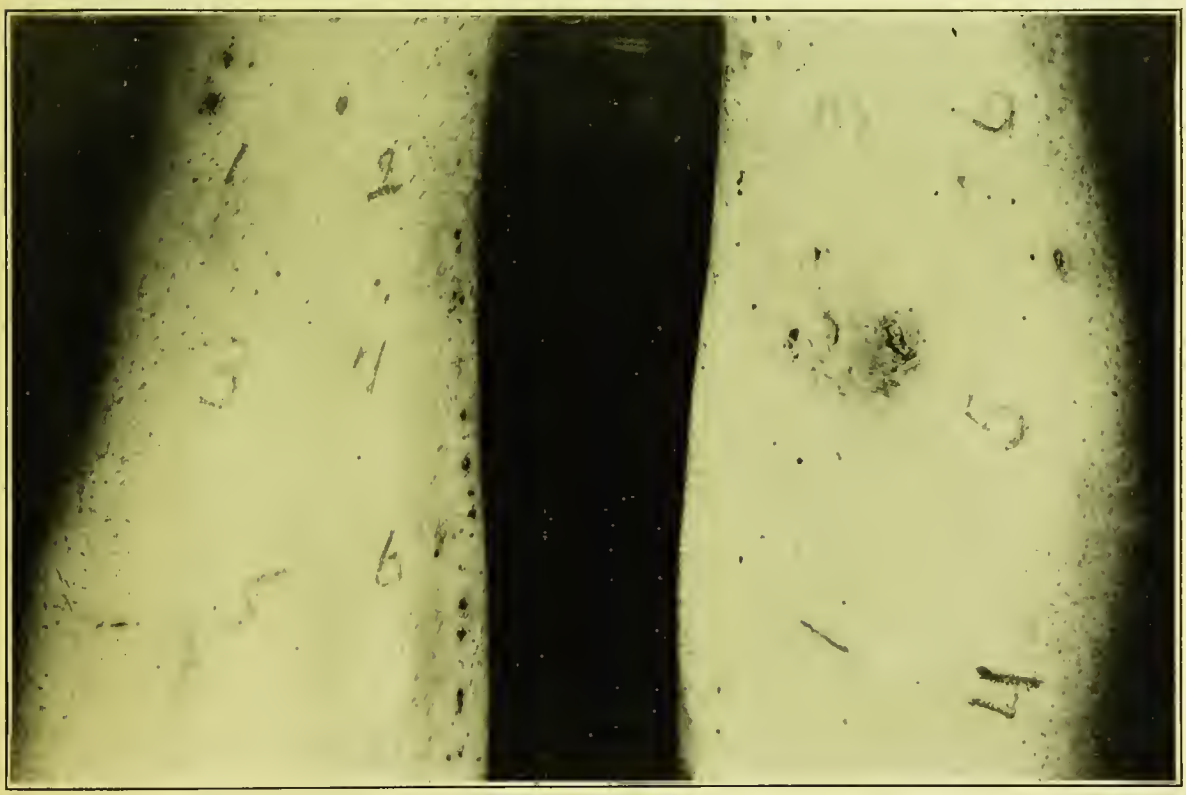
Figure 1. Method of pinching-up the skin to render the first puncture of the needle as painless as possible.

touch and deep soreness as though bruised by being struck by some blunt object. After three hours the blanching of the skin is replaced by capillary dilatation. The hyperesthesia continues to be marked for twenty-four hours or longer.

The various additions to the novocain-epinephrin mixture were investigated to determine their influence in prolonging the action of the novocain. Calcium chlorid and magnesium chlorid were tested out combined and separately, with and without the addition of trichlorbutanol as recommended by Harris.[1]

Novocain-epinephrin with calcium chlorid plus trichlorbutanol in its early action was like novocain-epinephrin (*3-Figure 2*) except that the momentary smarting, after the injection was first begun, was more intense. The *goose-skin* surrounded the injected area for 2 cm. on all sides. The anesthesia is complete in about the same time as in the case of the novocain-epinephrin solution. After an hour and a half anesthesia already begins to grow less. After three hours there was marked hyperthesia, but there was still some anesthesia but by no means complete, and there was also marked deep tenderness.

The same solution with the addition of magnesium chlorid makes no notable change in the onset or duration of the anesthesia (*4-Figure 2*).



Figures 2, 3. Method of mapping out areas in the comparative duration of local anesthetics. (3) Local necrosis intentionally produced at 2 by Isoamlhydrocuprein hydrochloricum.

The accessory drugs were then used alone The calcium chlorid plus trichlorbutanol (without novocain but with epinephrin) caused marked burning, when injected, with primary and persistent capillary dilatation, (*5-Figure 2*). Anesthesia was complete in about 20 minutes. Though there was capillary dilatation at the immediate site of injection, there was marked *goose-skin* in a zone about this area. This would seem to indicate that calcium chlorid-trichlorbutanol interferes with

the epinephrin at the actual site of injection and the epinephrin acts in an area beyond that acted upon by the calcium chlorid combination. The anesthesia was still present after an hour and a half. After three hours the anesthesia was gone and there was marked hyperesthesia, deep tenderness and marked capillary dilatation over the site of injection.

The same solution with the addition of magnesium chlorid gave no noticeable difference (*6-Figure 2*). On the averarge there seemed to be less pain on injection and the late deep tenderness seemed to be less. The site of injection was equally hyperdemic.

So far as the present discussion is concerned and others made in previous papers the following conclusion may be rendered: *Novocain used alone gives a very fleeting anesthesia and is not to be considered in the control of after-pain. With epinephrin the anesthesia may be counted on to last for two hours and for this time assures the patient freedom from after-pain. The calcium chlorid used alone produces anesthesia as quickly and lasts as long as the novocain but causes greater pain when introduced and is followed by greater hyperemia and more intense deep tenderness. The addition of magnesium chlorid makes no noteworthy difference, The addition of the accessory drugs above mentioned permits the use of a weaker solution of novocain, but this is secured at the expense of more discomfort during injection and more deep tenderness following injection. In small operations when the amount of solution used is small the accessory drugs are contraindicated, but when large amounts are required they may be added with advantage.*

These additions are not capable of prolonging the duration of anesthesia produced by novocain-epinephrin and are productive of a greater tissue reaction than the novocain-epinephrin alone. This may be objectionable when injected directly into the field of operation, though there is no evidence of the exact degree and nature of the tissue changes produced. When nerve blocking is resorted to the tissue reaction placed at some distance from the actual wound and this reaction is of no consequence as far as wound healing is concerned.

Schlesinger[2] tried out potassium sulphate and failed to secure any increase in duration of anesthesia. This conclusion is contradictory to those advanced by Hoffmann and Kochmann.[3] These latter authors were not always careful to compare like operations, failing thereby to take into account the different degrees of *after-pain* following the various operations. They were able, it may be said in passing, to reduce the novocain to 0.1 per cent. by the addition of potassium sulphate in the proportion of 20 cc. of the 2 per cent. solution to 100 cc. of the sodium chlorid-novocain solution.

The action of quinin and urea hydrochlorid being previously known this drug was tested out with the same collateral solutions as were used with the novocain-epinephrin. Quinin with sodium chlorid solution gave more pain than novocain-epinephrin but no more than novocain-epinephrin and calcium chlorid plus trichlorbutanol. The anesthesia with the quinin and calcium chlorid plus trichlorbutanol was complete as quickly as with novocain-epinephrin. The burning upon injection was intensified and the deep tenderness much increased. *To summarize these experiments it may be said that none of these accessory drugs is capable of mitigating or prolonging the effect of quinin anesthesia.*

Professor Morgenroth, of Berlin, was good enough to send me some new samples of quinin. I shall mention but one of these, Isoamyl-hydrocuprein hydrochloricum. This drug is active in 0.1 per cent. solution. It was tested with the accessory drugs already mentioned in the discussion of novocain. The addition of these drugs did not influence the effect of this quinin preparation but did add very materially to the deep tenderness. This new drug is followed by fibrinous infiltration as quinin and urea hydrochlorid is, though perhaps to a slightly less extent. It is possible to produce a necrosis with it if it is injected in excess (*2-Figure 3*). The necrotic area shown in the figure was produced by injecting 2 cc. of 0.2 per cent. solution at one point endermically.

The deep tenderness and hyperesthesia surrounding the infiltrated area is about the same. The conclusion I would draw is that this drug is about equal to quinin and urea hydrochlorid when used in solutions of 1-10 to 1-5 the

strength. The deep tenderness is about the same.

These studies failed to discover any drug at all in the class with quinin and urea hydrochlorid in producing prolonged anesthesia, and it is the only one worthy of consideration in the control of *after-pain.*

VITAL FACTORS IN THE PROBLEM OF PRODUCING ENDURING ANESTHESIA

The study of this drug therefore is imperative if we are to control *after-pain* by the use of local anesthesia. No other drug or combination of drugs in its class as pertains to duration of anesthesia. It would seem worth while to study more carefully some of the fundamental factors upon which the duration of anesthesia depends.

The strength of solution should not be less than 0.5 per cent. nor stronger than 1 per cent. Within this range there is no demonstrable advantage. The important factor is to remember the manner in which it acts. As previously stated,[4] the action of quinin upon the tissue is such that a granular fibrin is produced at the site of injection. This exudate remains in the tissues from four to eight days or longer, depending upon the kind of tissue in which it is placed and the facilities for absorption. The duration of anesthesia is generally coextensive with the presence of this granular fibrin in the tissues.

Were this the only factor to be considered the problem of producing enduring anesthesia would simply be that of injecting the anesthetic solution in sufficient amount. The chief point is to so place the solution that ligatures and sutures will fall into the actual region of fibrin deposit. Blocking a nerve in continuity with quinin and making ligations or sutures in the region so blocked will not meet with success. It is a failure to regard this point that has been responsible for the variable results reported.

In the first place the ligature may be so placed that the hyperesthetic zone is invaded. This may produce excruciating pain. This hyperesthetic zone, as is now well known, occurs regularly about the field of anesthesia and may extend into the field previously anesthetized. The cause of this hyperesthesia is not understood. The neurologist often notes a hyperesthetic zone above the anesthetic area in spinal cord lesions. We may assume that where the anesthetic has not acted upon a nerve with sufficient intensity to anesthetize it, it acts as an irritant heightening its sensibility.

Still more important is the return of sensation in the area blocked before the nerve supplying the area regains its sensation. It is possible that this return of sensation may be explained as Waldeyer explains the return of sensation in areas supplied by cutaneous nerves which have been severed. It is well known that the section of cutaneous nerves is followed by anesthesia in the region supplied by that nerve. Sensation in such an area may be regained long before the regeneration of the nerve is possible. Waldeyer explains this by assuming that collateral nerves learn to take up the innervation of the region previously supplied by the severed nerve.

This phenomena may be diagrammatically illustrated by assuming that in the operation for hemorrhoids by blocking the nerves in the ischio-rectal fossa as at *D Figure 4,* the hemorrhoid B supplied by that nerve becomes anesthetic by this infiltrated area C, and may be operated on painlessly. Within a short time twigs from nerves E and F take up the innervation of the area, previously supplied by the nerve D through anastomosing branches.

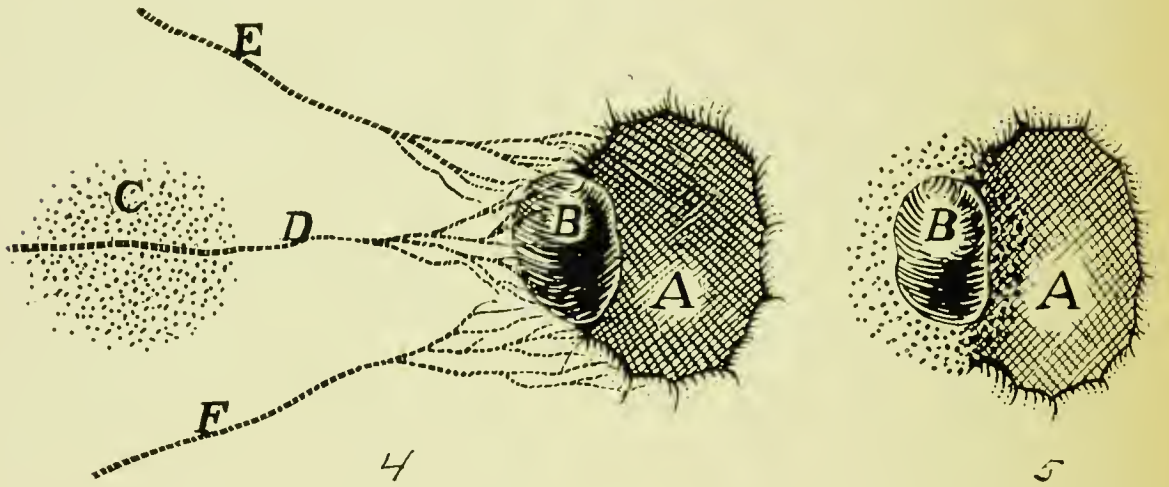
A direct argument in favor of this hypothesis is observed in sacral blocking with quinin for rectal operations. By this means all the nerves going to the area in question are blocked at their source, making it impossible for sensory impulses to escape by collateral nerves. Be this as it may, the fact holds that ligatures must be made in tissues actually infiltrated. In order to secure enduring anesthesia in hemorrhoids it is necessary to infiltrate the hemorrhoid directly, as is represented by the dotted area about the hemorrhoid *B in Figure 5.* By following this rule constant results may be obtained.

The injurious effect of quinin upon the tissues must not be forgotten. Numerous observers have proven that it is possible to produce disturbances in wound healing by the use or abuse of quinin. The question then

offers itself as to when the use of quinin for the control of *after-pain* is justified. In hemorrhoids where the pain is severe and the wound disturbances unimportant, and in digital suppurations where all the nerves can be blocked at some distance from the seat of suppuration gratifying results may be obtained. Blocking of nerves in amputations may be done with impunity. Sacral blocking in extensive operations about the rectum and prostate seems well worth while in many instances. In other regions the pain is often not great and the local anesthetic can at most but control the wound pain.

ing moment. When blocking is resorted to, unless the blocking secures all nerves going to a given part, the more quickly acting novocain is equally as effective.

The use of local anesthetics for the control of *after-pain* when general anesthesia is employed has as yet no basis in fact. Except in a few instances as in the ligation of hemorrhoids after more formidable operations under general anesthesia, as first practiced by Ford Rogers, has but a slight value and anything like a broad application has not yet been worked out. Allen is quite in accord with my own conclusions repeatedly expressed when he declares



Figures 4, 5. Diagramatic representation of how sensation from collateral nerve fibres provokes the return of pain before the evanescence of desenzitation from nerve blocking. (5) Showing how after-pain in a localized area is more thoroughly controlled by infiltration.

The complicating pains, notably gas pains, are not controlled by local anesthetics. Gas pains come as readily after local as after general anesthesia when the abdominal cavity is invaded. This applies to operations done under local anesthesia alone or when combined with general, considering of course that operations of equal magnitude are compared.

Admitting the greater convenience of novocain-epinephrin in routine work, the question arises as to when quinin should be used merely for the sake of the more adequate control of *after-pain*. In very painful areas, as in those noted above, quinin should be the anesthetic of choice. For the majority of operations the after-pain is not so great as to be of command-

against the use of quinin in the peritoneum after the abdomen is opened merely for the control of *after-pain*.

The literature relating to the duration of anesthesia after the use of quinin is neither extensive nor impressive. The bare references found in the literature do not give the evidence upon which the conclusions of the writer are based. A few of these may be quoted. Lispmasse[5] states that anesthesia lasts up to twelve hours. L. Eliot[6] writes that anesthesia lasts up to several days. W. O. Green[7] secured anesthesia lasting twelve days in a case of hemorrhoids. C. W. Allen[8] gives instances of analgesia lasting ten to twelve days. Thaibault[9] describes anesthesia lasting one to six

hours. Crile in employing it in the peritoneum for the control of after-pain does not, in any of his numerous publications on the subject, make any statement as to how he knows anesthesia is actually produced, nor does he give any information as to how long the anesthesia lasts. Other quotations would only emphasize the uncertainty of the duration of the anesthesia following the use of quinin. Harris [10] states that because of its uncertainity he has given up its use.

Inasmuch as in quinin alone, among all known drugs, is there any hope of the control of after-pain, it is worth while to inquire into the failure of the drug to gain a wide use.

AVOIDING COMPLICATIONS IN THE USE OF QUININ-UREA HYDROCHLORID

The chief positive cause is the fear of producing necrosis. One of the first warning notes was sounded by Wyeth. He had two cases of sloughing following deep injections. One of the most interesting unfavorable results reported is that by Allen. He used seven ounces (that is nearly half a pint) in a hernia. Sloughing resulted. He states that the hernia was a large one. That goes without saying. If it had not been very large indeed it would have been mechanically impossible to have gotten so much fluid around it. In every case of necrosis reported, in which I have investigated the details, the amount of fluid used has been far beyond the requirements, and in many cases tissues were injected that should never have been injected by an anesthetic. Obviously these details secured through private sources are not available for publication. In no case has necrosis followed the use of quinin where the injection has been properly made. Suppuration of the wound may follow any technic, and the excessive use of any local anesthetic, and it occurs more particularly after quinin than after novocain. If quinin were not safe in large amounts there would be less disposition to use it *ad libitum* and these unfavorable results would soon cease to occur.

The histo-chemistry of quinin when injected in the tissue has already been dealt with on several occasions and need not be repeated here. I do believe that a proper technic in the use of quinin will be acquired until the surgeon acquaints himself with this reaction of the tissues to quinin.

The uncertainties in the action of quinin is a problem not fully solved. They hinge about the problem of zonal hyperesthesia, to which attention has already been called, and a failure to properly infiltrate just those tissues from which the painful impulses originate.

When estimating the power of local anesthesia to control *after-pain,* when used alone or in conjunction with general anesthesia, the pain produced by the action of the local anesthetic upon the tissues must not be forgotten. In most instances this added irritation is inconsequential, but in some regions this factor is important. So little attention has been given to this phase of the problem that little of value can be said regarding it. Schlesinger has made the suggestion that the pain due to the anesthetic and that due to the operation itself does not account for all the after-pain. In other words, the two associated interact upon each other augmenting the simple addition of both. Those who have studied the problem are pretty generally in agreement that there is less after-pain when the operation is done by nerve blocking. This applies only of course when novocain is the anesthetic used. This is also true when novocain is used with the accessory drugs above mentioned. When novocain-epinephrin alone are used there is little difference in tissues not the site of inflammation.

It is worth while to remember that all local anesthetics themselves cause some injury to tissue, and that the injury to tissue by the drug itself and by the needle used to introduce it are factors to be regarded. If this is remembered, gentleness in the manipulations of injection and the use of a minimum amount of fluid will be the goal.

The technic of the operation under local anesthesia has much to do with the sum total of after-pain. So far as local anesthesia is concerned its chief contribution is the interpretation of those factors which produce after-pain thus making it possible to avoid them.

The method of avoiding those due to the anesthetic itself has been sufficiently set forth. The service of local anesthesia as it relates to after-pain, however, is in compelling the oper-

ator to gain a practical knowledge of neural anatomy and to teach him the lesson of gentleness. This acquired, he has but to follow the simple rule of avoiding the tissues which are sensitive when he makes his ligations and passes his sutures.

From the foregoing it becomes apparent that up to date but little worth while is known about the control of after-pain by local anesthetics. This is due in part to the fact that surgeons have not given the matter much thought, and partly from the lack of an ideal drug that can be used for this purpose. The employment of quinin for this purpose gives some promise of success, but as yet is far from ideal. With the increased use of quinin this end may be attained with more and more gratifying results. The use of quinin must be made incapable of abuse and there must be developed a technic that will insure constant results.

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ONE OF THE MOST SALIENT CHARACTERISTICS OF MODERN LIFE, IS THE INCREASING AMOUNT OF LEISURE TIME FOR RECREATION MADE POSSIBLE BY THE SHORTENING OF WORKING HOURS. THE ADVENT OF SPECIALIZATION, LABOR-SAVING DEVICES, THE TELEPHONE, TELEGRAPH, AND AUTOMOBILE MAKE IT POSSIBLE FOR ALL CLASSES OF PEOPLE TO DO MORE WORK IN LESS TIME THAN BEFORE. BUT WORK IS MORE INTENSIVE AND CONSEQUENTLY MORE FATIGUING. THE RESULT OF THESE CHANGES IS, A GREATER NEED FOR RELAXATION AND MORE TIME AVAILABLE FOR RECREATION AND PLEASURE. THE PROPER USE OF LEISURE TIME HAS MUCH TO DO WITH HEALTH, EFFICIENCY AND HAPPINESS. PLAY IS GENERALLY CONSIDERED AS BELONGING TO CHILDHOOD ONLY, BUT IT IS REALLY A VITAL PART OF LIFE AT ALL AGES.

—*George F. Butler.*

ANO-RECTAL OPERATIONS UNDER LOCAL ANESTHESIA . GENERAL CONSIDERATIONS . PREPARATION OF THE PATIENT . INSTRUMENTARIUM AND SOLUTIONS . OPERATIONS ON HEMORRHOIDS . TECHNIC OF ANESTHESIA FOR OBTUNDING SPHINCTERIAN NERVES . OPERATION FOR ANAL FISSURE AND ANO-RECTAL FISTULA . SUMMARY

BY LOUIS J. HIRSCHMAN, M. D., F. A. C. S. *DETROIT, MICHIGAN*

IN THE WHOLE FIELD of entero-proctologic surgery there is no class of operations in which so much progress has been made through the employment of local anesthesia, as in those procedures which involve the surgical relief of diseased conditions of the anus and lower rectum. Certain facts about local anesthesia in general are so well estabished that it is not necessary at this time to enter into any argument regarding its desirability, safety, or adaptability in a large and expanding field of usefulness.

While local anesthesia has been employed with varying degrees of success in many other branches of surgery, nowhere has its employment been so welcome or has it achieved such glory in advancing a specialty, as it has in proctologic surgery.

GENERAL CONSIDERATIONS

The unwarranted fear of hospital detention, general anesthesia and the use of *the knife* has been fostered by the glaring advertisements of the irregular and advertising quack to the great dismay of the sufferers from ano-rectal diseases, with the result that they have been enticed in great numbers in the past by these charlatans and have been exploited *for revenue only*.

The fact that one occasionally learns of the death under general anesthesia of some individual who had submitted to a simple operation for fissure or hemorrhoids, has also stimulated a search for some anesthetic agent or procedure which would render a comparative minor operation free from the added dangers of a general anesthetic.

To-day there is no field in medicine or surgery where the employment of local anesthesia has resulted in more brilliant achievements than in the field of surgical endeavor covered by the proctologist. For nearly a decade and a half the author has been employing local anesthesia in the surgical treatment of the majority of his cases of anal and rectal surgery as well as in a smaller proportion of cases involving surgery of the colon.

The results in his personal experience involving thousands of these cases have been so satisfactory to both himself and his patients that he advocates with great earnestness the further employment of local anesthesia not only in ano-rectal surgery but also in other branches of surgical activity where absolute unconsciousnes of the patient is not a strict necessity.

For the successful employment of local anesthesia in the surgical treatment of any disease there are several essentials which must be rigidly observed.

One must be sufficiently familiar with the contraindications to the employment of local anesthesia in order to carefully select his cases. The temperament of the patient; the surroundings in which the operation is to be performed; the nature and extent of surgical operation; the length of time it will probably consume; the individual idiosyncrasy of the patient to certain anesthetic drugs; and lastly and perhaps most important of all, the psychic surroundings as governed by the surgeon himself.

The mental attitude of the surgeon and his

assistants; the way in which he approaches his patient; his conversation with the patient before and during the operation—in fact, his general handling of the case has as much to do with the success of the employment of local anesthesia as had the selection of the kind and quantity of anesthetic used.

While it is true many operations on the anus and rectum can be and are performed with entire success in the office operating-room or in the home of the patient, it is far better for every operative procedure, no matter how apparently minor it may seem to the surgeon, to have his patient in a well-equipped and well-conducted hospital.

To the surgeon, the many reasons for this are obvious. The patient should understand that the surgeon can do his vary best work when he has at his command all of the advantages which a modern hospital affords.

It is not the author's purpose to enter into a long discussion of all the various operations which may be performed in the ano-rectal region under local anesthesia, but to briefly describe the operative details of the simplest technic with which it is possible to get good results.

Suffice it to say, however, that many a patient is suffering permanent injury by submitting to so-called non-surgical methods of treating ano-rectal diseases in the hands of the charlatan, because of the fear in his mind of the *surgeon's knife, general anesthesia, and hospital detention.* Also many a patient is suffering unnecessary discomfort, pain and lessened efficiency because of the untreated diseases of the rectum from which he is suffering on account of his unwillingness to submit to a general anesthetic. Then, too, there are many cases of recurrences following operations under general anesthesia by surgeons who, while perhaps skilled in surgery generally, have not a specialized knowledge of the requirements of a successful ano-rectal operation.

It has been the author's experience to hear the surgical treatment of rectal diseases, hemorrhoids particularly, decried by patients who had submitted to various operations, for their relief because of the fact that they were not thoroughly and properly performed. The author will mention the reasons for these recurrences in discussing the technic in operating for internal hemorrhoids under local anesthesia.

Practically every operation with the exception of the dissection of extensive fistulas and the extirpation of dense rectal strictures or cancer, can be performed successfully by the skilled rectal surgeon under local anesthesia.

GENERAL PREPARATION

In preparing a patient for any operation, under local anesthesia, one should be just as thorough as for a similar operation under complete general anesthesia. For at least twenty-four hours before the operation the patient should be limited to a fluid and assimilable diet. His bowels should be thoroughly emptied by means of a liberal cathartic given 24 hours before the time selected for operation. On the preceding evening and the following morning a cleansing enema should be given. The perineum should be cleansed the night before the operation and protected with sterile dressings.

There is no objection to a cup of hot coffee or a glass of milk an hour and a half before operation. In fact it is the author's custom to administer from 15 to 20 grains of chloretone and 1-4 grain of morphin with a glass of hot milk or a cup of coffee an hour or an hour and a half before operation. In lieu of this a half hour before operation, 1-4 grain of morphin with or without 1-100 grain of scopolamin may be administered hypodermically.

The patient is kept as quiet as possible, relatives not being allowed in the room to converse with him before operation. If he becomes thirsty, there is no objection to his drinking a few ounces of water before going to the operating-room.

Of prime importance is the arrangement of the operating-room. The success of an operation under local anesthesia may be entirely nullified by the lack of attention to the surrounding details.

The strict observance of silence by all who come in contact with the patient is extremely essential. This means that the operating-room should be fully prepared before the patient is brought in. There should be a minimum of nurses bustling around handling dishes, instru-

ments and utensils, and what conversation is imperative should be carried on in a subdued tone.

The author employs a code of signs and signals largely, instead of asking for his instruments, or dressings, and thus minimizes the amount of necesary conversation.

The operating table should be covered with a thick pad or mattress, which should be warmed and all instruments, gauze, and paraphernalia kept out of the patient's sight at all times.

The internes and assistants should always bear in mind the fact that the patient is *not asleep* and that every touch is felt by him, and the patient at all times should be handled as little as possible and when handled at all, only with the utmost gentleness and care.

The patient's ears are stuffed with cotton and a towel placed over his eyes. Pillows are allowed, in fact anything which will make him comfortable, and he is not restrained, tied or strapped in any way.

SOLUTIONS AND INSTRUMENTS

The solution used for anesthetizing the skin is one-eighth of one per cent. beta-eucain lactate or novocain. A 30 cc. all-metal or all-glass syringe (Figure 1 A), is filled with warmed anesthetic solution, and after the skin has been touched with phenol or pinched for a moment, it is punctured with a quick thrust of the hypodermic needle. This needle, by the way, should be sharp and of at least 26 guage.

Quinin-urea solution is not used for injecting the skin because its injection is painful, while the eucain or novocain is quickly absorbed and does not affect the healing of the skin. In the deeper structures, this infiltration with quinin and urea does not interfere with healing at all.

Above all things when an operation under local anesthesia is to be performed, the surgeon must not be in too much of a hurry to start his operation after injecting the anesthetic. One should wait at least 5 minutes after injecting eucain or novocain before incising the skin and in order to achieve the best results in the way of postoperative anesthesia when using quinin and urea, one should wait at least 10 minutes after injection before incision. The failure to produce satisfactory anesthesia in most surgeons' hands, has been

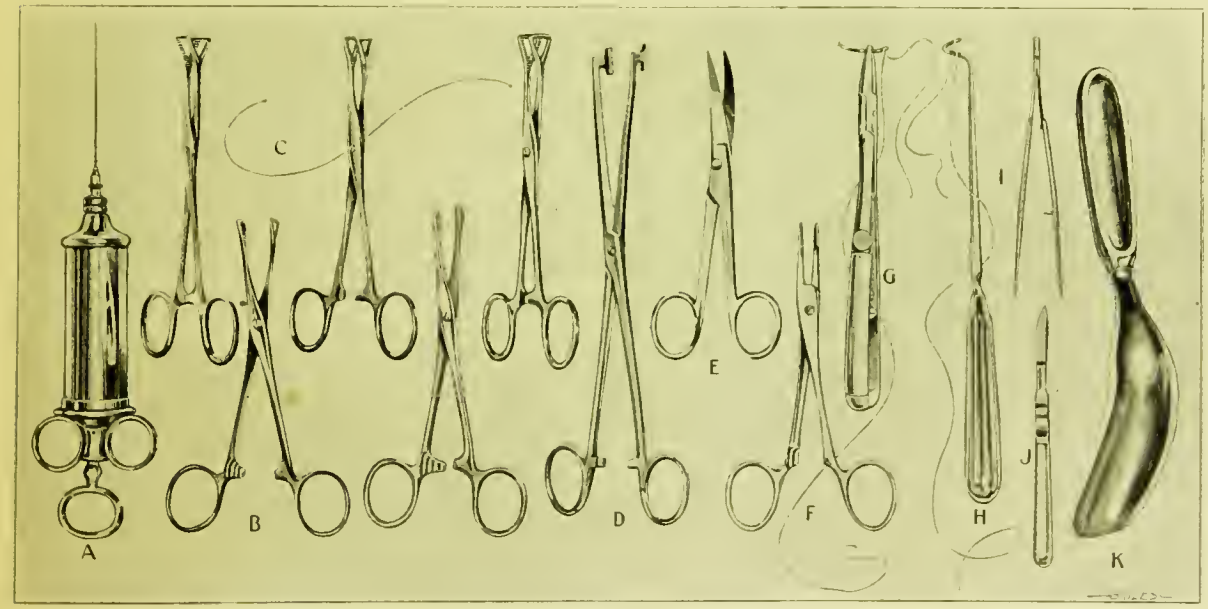


Figure 1. Instruments for ano-rectal surgery under local anesthesia. (A) 30 cc. all metal syringe; (B) Pennington triangular forceps; (C) annealed silver wire; (D) Hirschman pile forceps; (E) sharp-pointed scissors curved on flat; (F) sharp-pointed hemostatic forceps; (G) full-curved round needle with No. 2 catgut tied in eye; (H) Hirschman's ligature carrier threaded with No. 2 catgut; (I) tissue forceps; (J) small scalpel and (K) rectal retractor.

Figure 2. Case of prolapsing internal hemorrhoids suitable for operation under local anesthesia.

Figure 3. Point of puncture for anesthetizing the posterior sphincterian nerves.

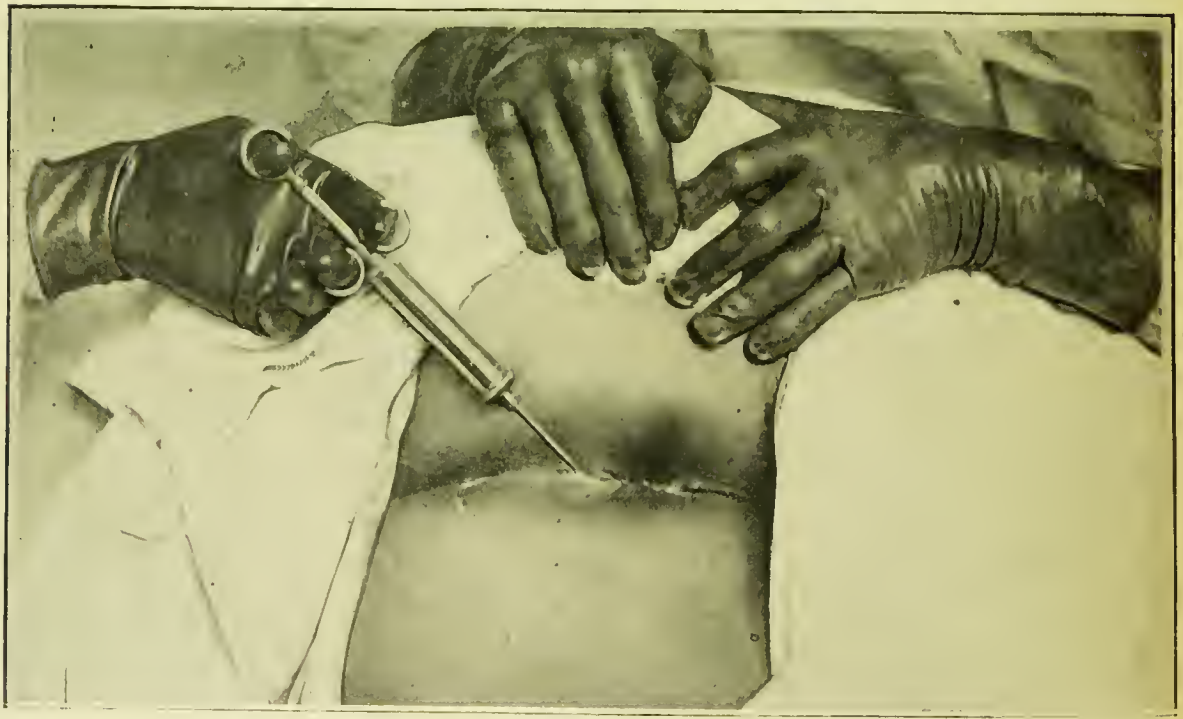


Figure 4. Exact point of puncture for anesthetizing anterior sphincterian nerves.

Figure 5. Amount of distention necessary to anesthetize anterior and posterior sphincterian nerves.

due to their anxiety to start the operation before full and complete local anesthesia has been produced.

OPERATIONS ON HEMORRHOIDS

What will now be said regarding technic of hemorrhoidectomy is equally applicable to all other operations in this region.

The patient is placed in the left lateral position, which is most comfortable for him as well as the surgeon. After the parts have been cleansed and rendered aseptic, a point one-half inch posterior to the posterior anal commissure (Figure 3) and a similar point at the anterior commissure (Figure 4) is touched with a swab moistened with phenol. The injection of the one-eighth of one per cent. eucain lactate solution, is begun at the posterior commissure at the point touched with phenol.

With the index finger in the anus, gently hooking the sphincter downward, the injection is slowly carried around laterally, just underneath the skin about one-third of the circumference of the anus on both sides (Figure 5). About one drachm of the solution is slowly injected on the right side, then the needle is retracted to the point of puncture but not withdrawn, but is passed up on the left side of the anus in the same manner, keeping about one-half inch away from the anal aperture. This blocks the inferior sphincteric nerve and branches.

The anterior one-third of the anal circumference is treated in like manner, blocking the anterior sphincteric nerves. Then from the anesthetized areas, the remainder of the circumference of the anus is injected. The injection should be carried deep enough so that the needle enters and passes through the external sphincter both anteriorly and posteriorly and should also include the internal sphincter.

In external hemorrhoids the skin tags should

Figure 6. The extent of dilation which can be obtained under local anesthesia. Note how the internal hemorrhoids prolapse into full view without any instrumental help.

be distended until they are of a waxy white color (Figure 12). The pressure edema produced by the weak anesthetic solution is of more value in producing anesthesia than the amount of anesthetic salt used.

After waiting three or four minutes for anesthesia to become complete, the injected skin at the edge of the anus is grasped at the four points of the compass with the Pennington triangular forceps (Figure 1 B).

Traction on these four forceps everts the anus and prolapses the hemorrhoids if they have not already presented themselves (Figure 7). Slight expulsive efforts on the part of the patient at this time will assist in extruding the hemorrhoids.

These, starting with the most dependent one, are now injected with one-half of one per cent. solution of quinin and urea hydrochlorid. Sufficient of the anesthetic solution must be used to distend them thoroughly (Figure 8). The injection must be carried up to one-half inch beyond the junction of pile with healthy mucous membrane. Ten minutes must be allowed to elapse before any operation is started if one wishes to secure good post-operative anesthesia.

It will be noticed that the author has said

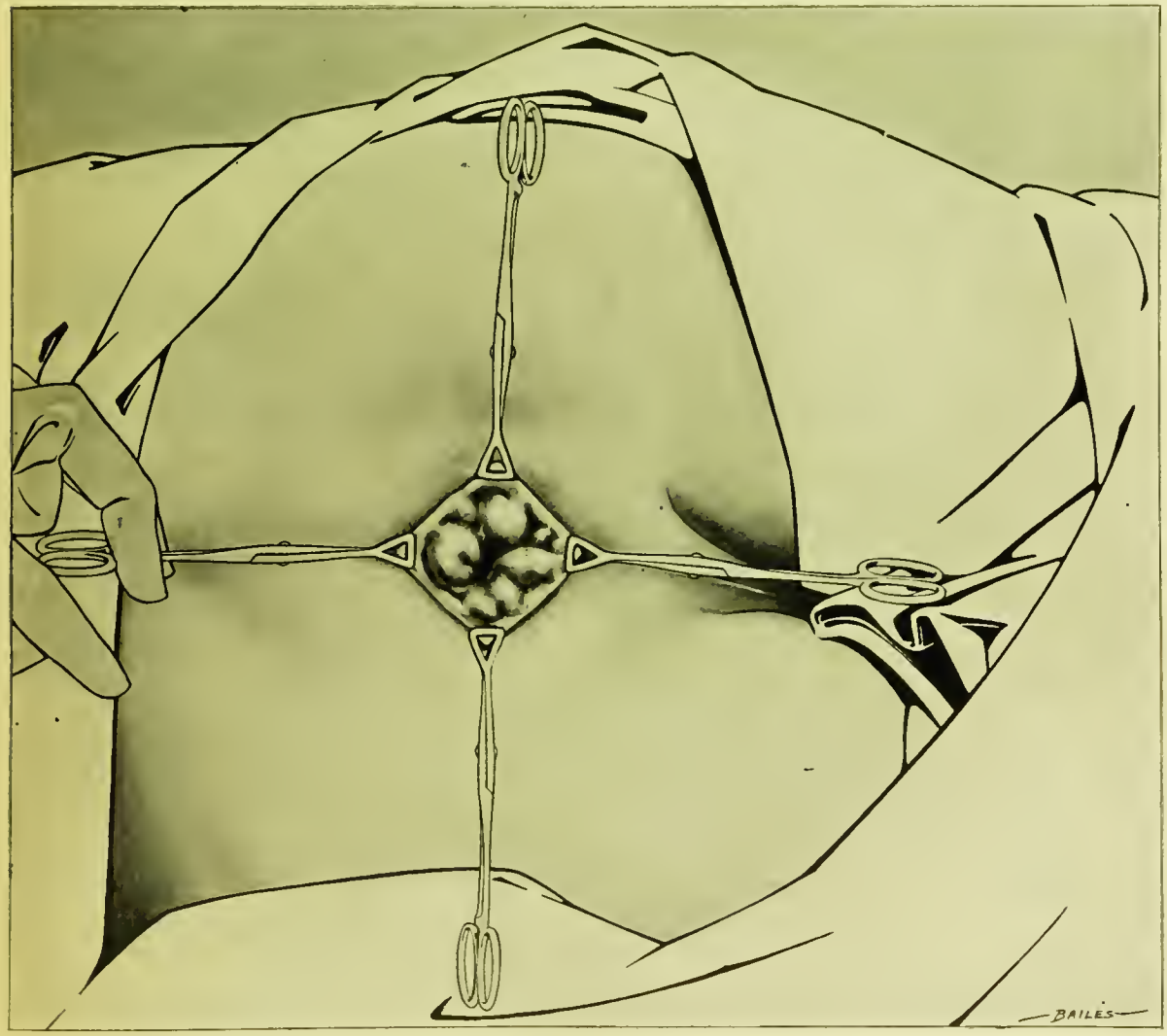


Figure 7. Internal hemorrhoids exposed by eversion of the anus with Pennington triangular forceps at four points of the compass.

nothing about the use of the rectal speculum, or has anything been said about dilating the sphincter. If one's technic is properly carried out in injecting the sphincterian nerves, the sphincter relaxes without any effort on the part of the surgeon to dilate it (Figure 6), and by the use of the four everting forceps the entire operative field is exposed in a much more satisfactory manner than could ever be accomplished by any retractor or speculum devised (Figure 7).

After ten minutes have elapsed, the hemorrhoids can be painlessly removed. The author's operation, which of course can be used under general anesthesia as well as under local anesthesia, if performed as follows:

First, the hemorrhoid is seized with the author's pile forceps (Figure 1 D), and drawn down in its long axis, then a right-angled curved blunt-pointed ligature carrier threaded with number two twenty-day chromic cat-gut (Figure 1 H), is passed into, underneath and around the hemorrhoid at its juncture with healthy mucosa (Figure 8).

The ligature is tied securely, one end being left fourteen inches long and the other five or

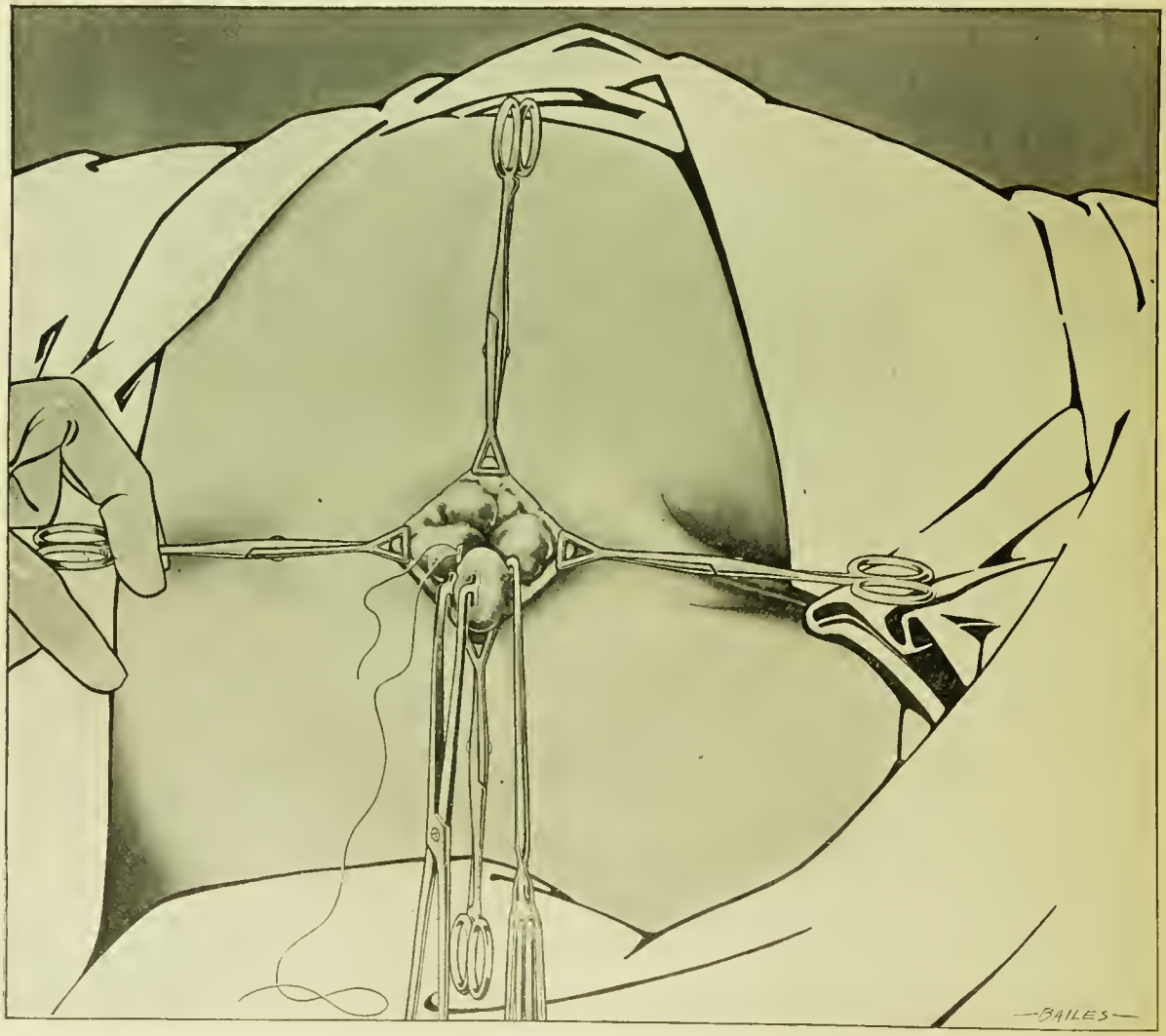


Figure 8. Hemorrhoids distended with anesthetic solution and ligature being placed under and around blood vessels.

six (Figure 9). All of the hemorrhoids are dealt with in like manner before any excision is attempted. By ligating all of the hemorrhoids in this manner before removing them, operative hemorrhage is reduced to a minimum.

We then return to the most dependent hemorrhoid which was first injected and ligated. This is again seized with the author's pile forceps (Figure 10), and is excised from without inward, care being taken to remove the presenting pile mass with as little mucosa as possible, and yet excise all that is redundant. The pile is then cut away one-quarter of an inch from the ligature (Figure 10), the ligature being held towards the side of the patient, opposite to the hemorrhoid. This keeps it above the wound and out of the way so that it will not be accidentally cut.

Then with a pair of small curved hemostatic forceps (Figure 1 F), the diseased vessels which form the bulk of the hemorrhoid below the level of the healthy rectal mucosa, are carefully dissected out, their exposure being assisted by upward pressure of the surgeon's finger on the outside skin beneath the hemorrhoid. All diseased tissue and veins are removed down to the sphincter muscles.

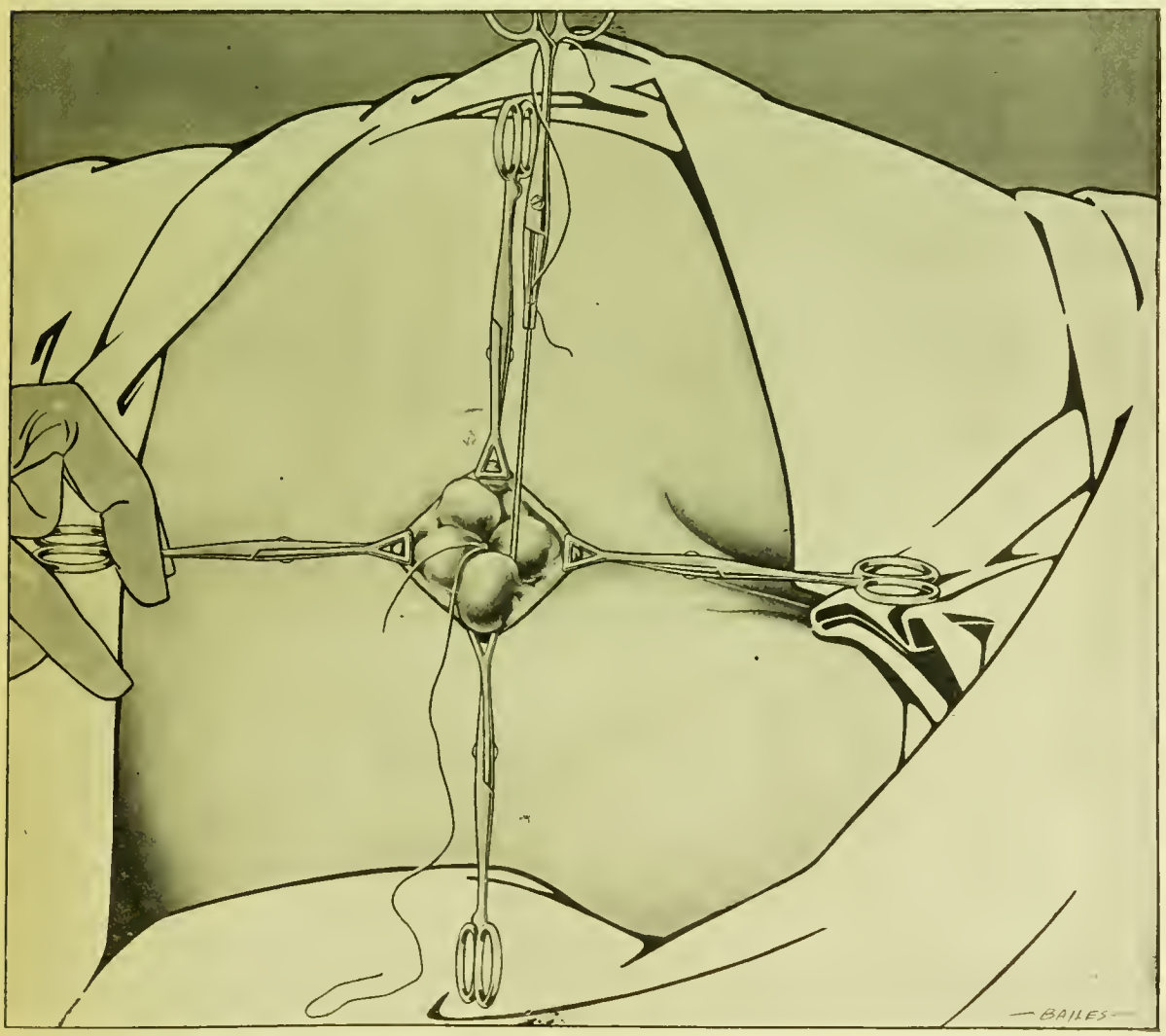


Figure 9. Ligature tied, leaving long and short end.

The long end of the ligature is then threaded into a small round full-curved needle (Figure 11), and the wound closed with a running suture. This long end is now tied to the short end of the combined ligature and suture, which is used chiefly for hemostatic purposes.

The other hemorrhoids are dealt with in like manner. The one at the upper part of the wound, that is the right side of the patient as he lies in the left lateral position, is left to the last. An injection of the quinin and urea solution is then made under the lines of suture for post-operative anesthesia, a dressing applied (Figure 16) and the patient sent to bed.

This technic is very simple and is efficacious for the following reasons:

(1) The anesthesia is complete and satisfactory.

(2) There is no necessity of damaging the sphincter by dilating or divulging it by mechanical means.

(3) By the everting forceps the use of specula, which only obstruct the view, is obviated.

(4) The method of placing the ligature at the junction of the pile and healthy mucosa by shutting off the blood supply from the branches of the superior hemorrhoidal vessels, renders the operation almost bloodless. The

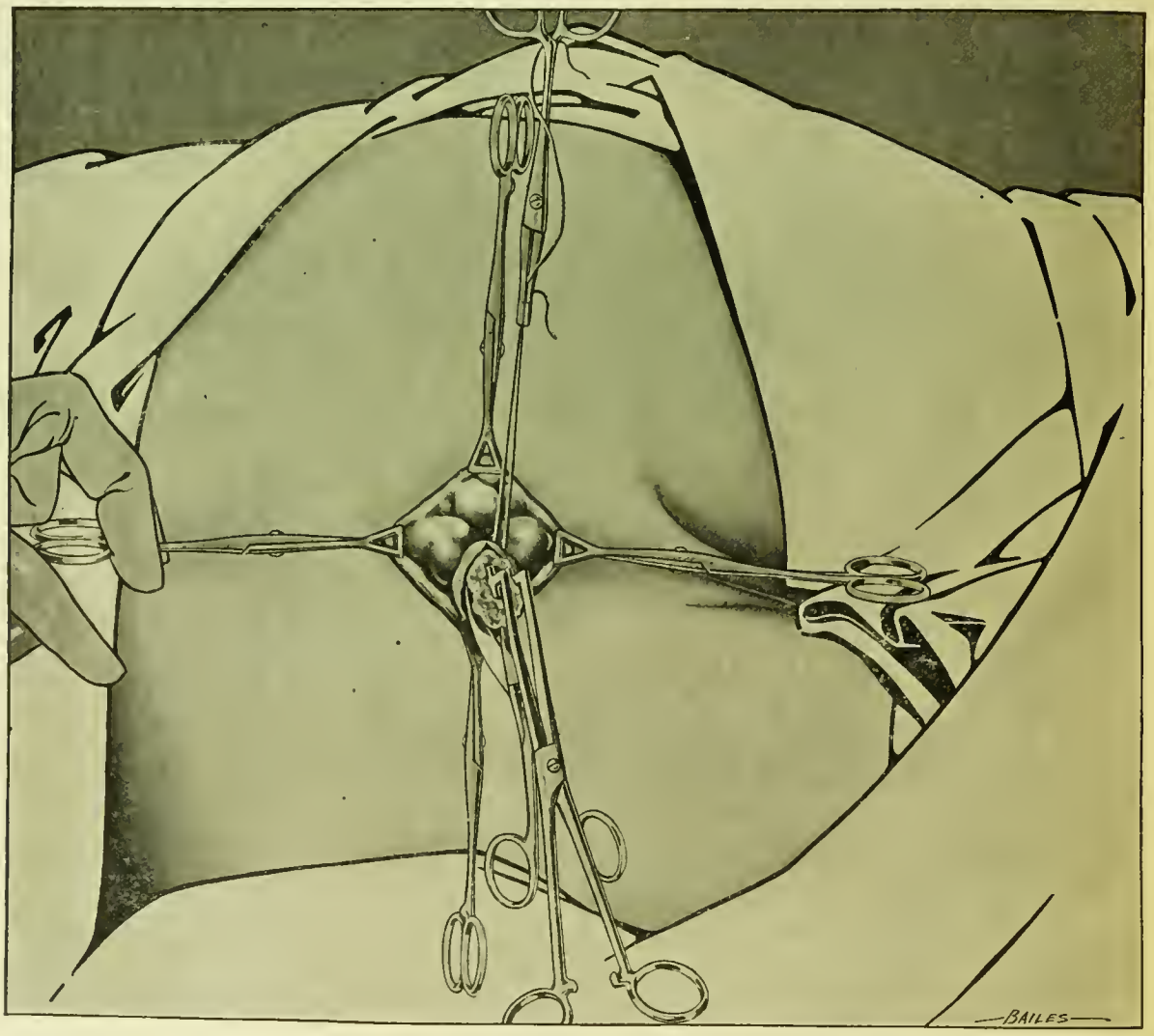


Figure 10. Submucous excision of hemorrhoid. Note how the ligature is held to the side opposite the hemorrhoid to prevent its accidental cutting.

only hemorrhage one meets comes from the lower portion of the wound which is largely supplied by the inferior hemorrhoidal vessels and is of no consequence.

(5) By tying the ligature with a long and short end, the long end of the ligature is used as a suture (Figure 11), and when tied to the short end at the top of the wound, brings the edges together so that good hemostasis is assured.

(6) By excising the hemorrhoid and removing all diseased tissue below the mucous level and down to the sphincter *all* of the pathology is eradicated and recurrence is impossible. The clamp-and-cautery or clamp-and-suture operations are so often followed by recurrence because only the top of the hemorrhoid is removed. All under the bite of the clamp is left behind and that very often is the major part of the hemorrhoid. By the open operation and the excision, nothing can be left behind and all of the hemorrhoid is accounted for. If the average surgeon who uses a clamp would before he sews or sears, remove the clamp, opening the wound and discover what he leaves behind, the author is sure there would be no

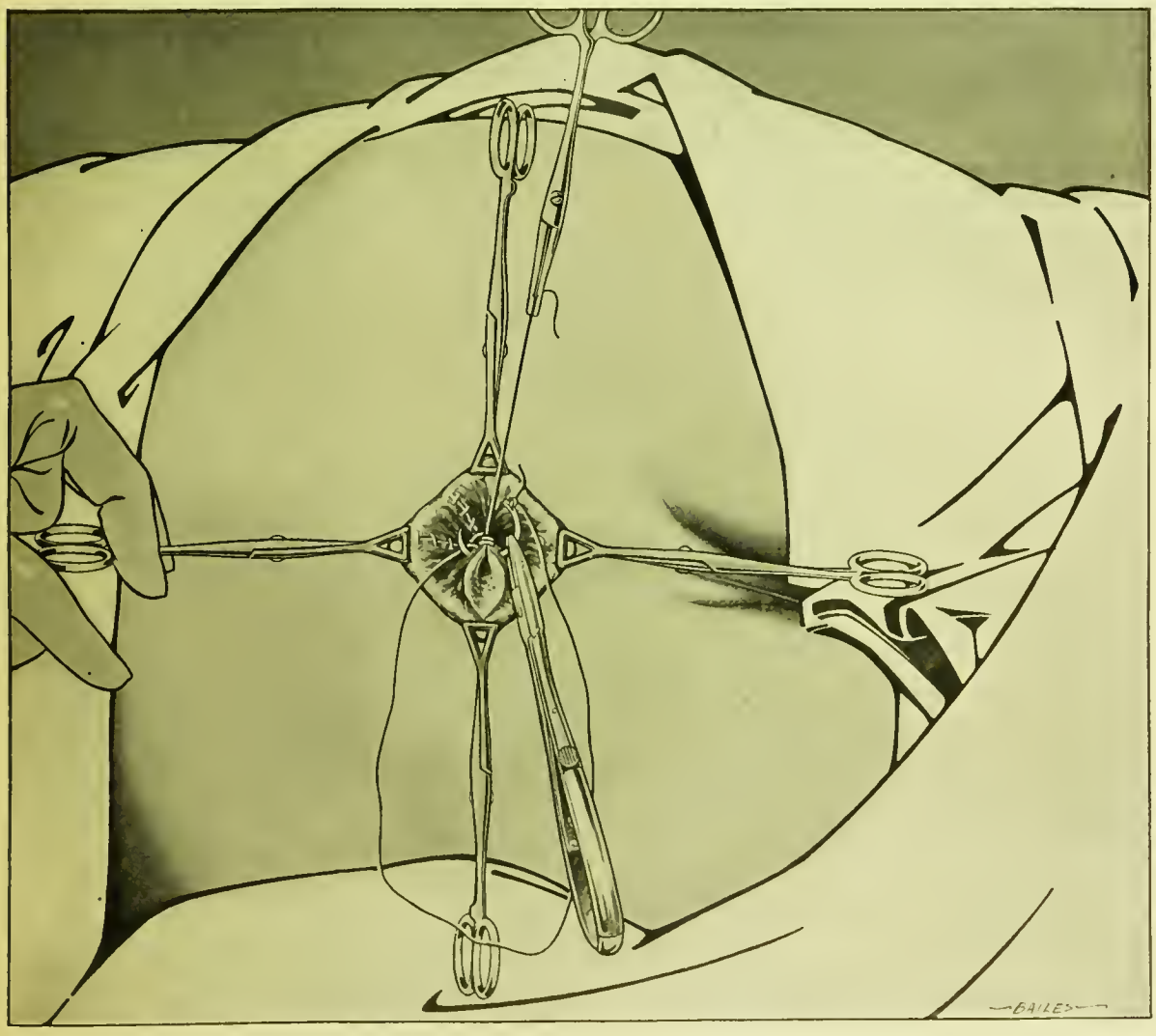


Figure 11. Incision being sutured, using the long end of the ligature tied in the needle as a suture. Note conservation of mucous membrane.

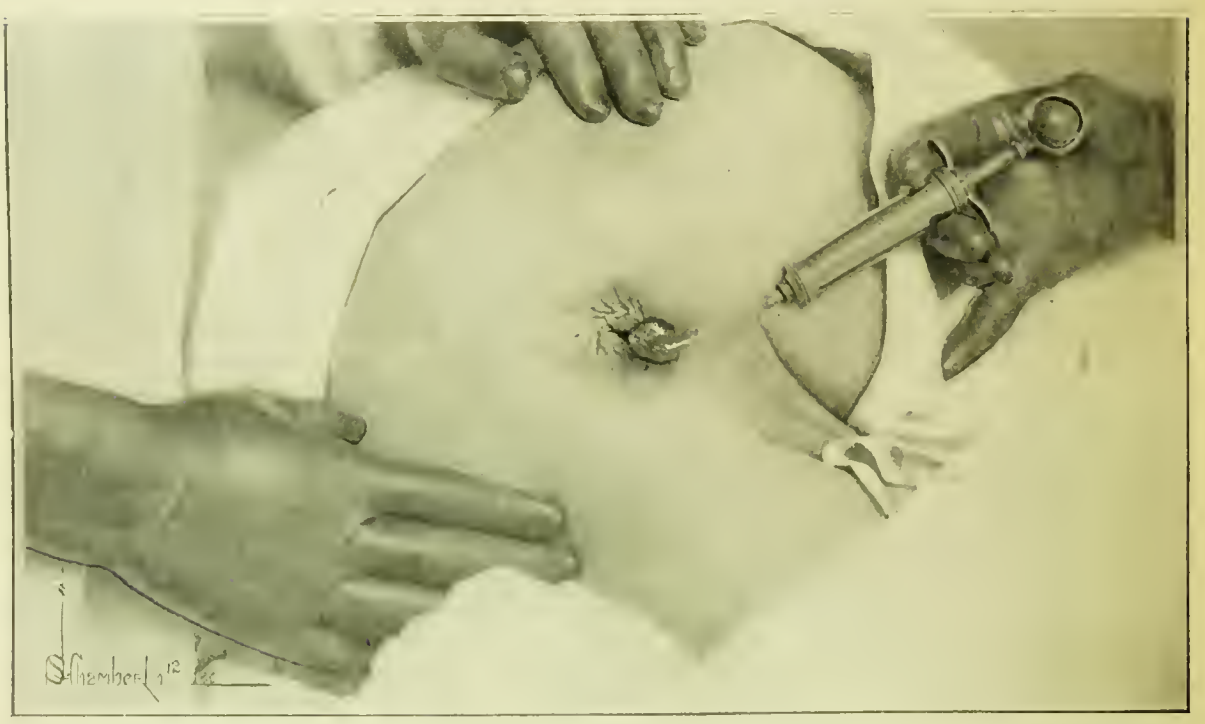


Figure 12. Anesthetizing external hemorrhoid.

Figure 13. Interno-external hemorrhoid anesthetized and ready to be excised.

more clamp operations performed for the removal of hemorrhoids.

(7) Post-operative anesthesia is so satisfactory when quinin and urea is employed, that the patient is able to be up and around after the first day or two, and many of them refuse to stay in bed at all.

(8) The lateral position prevents any sacro-iliac strain which is so often caused by the lithotomy position.

OPERATION FOR ANAL FISSURE

The use of local anesthesia in the operative treatment of anal fissure is so satisfactory that in the author's practice, a general anesthetic is never employed for this operation.

A fissure is an elongated ulcer of the anal canal, which by its in-folding has erroneously been called a split or crack and so designated (Figure 3). The principle involved in the treatment of fissure is the putting of the sphincter muscle at rest, at least that part of it involved by the fissure.

We were taught formerly that the best way to treat an anal fissure was to administer a general anesthetic and divulse the sphincter muscles. It is true that this procedure did relieve some cases of fissure, but it was a brutal and unnecessarily damaging method of putting the sphincter at rest. We now know that divulsion of the sphincter really means tearing the fibres of this muscle.

How much more rational, scientific and sur-

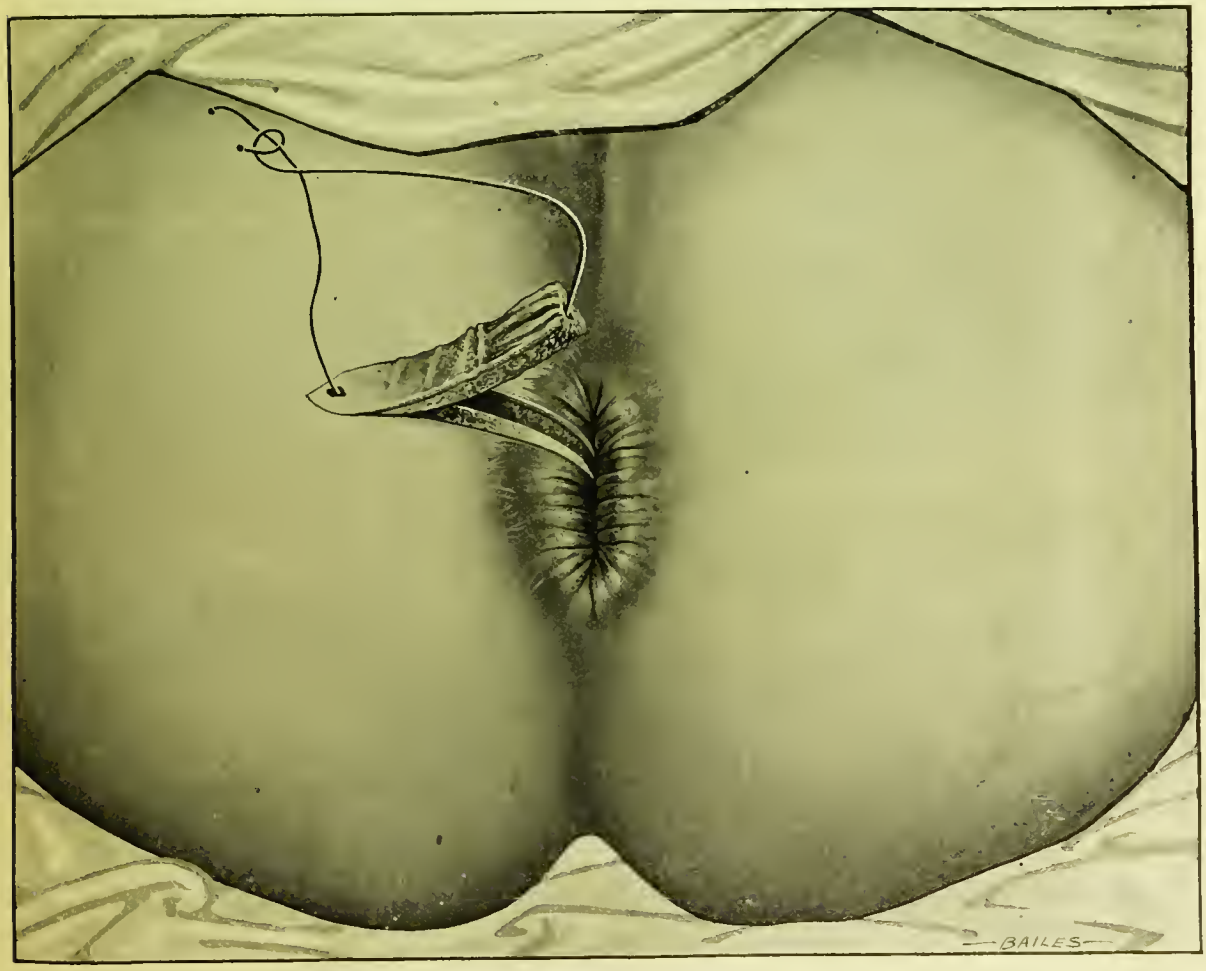


Figure 14. Method of dissecting out fistulous tract threaded on a silver wire probe, used as a tractor.

gical it is to put that muscle at rest by a clean-cut incision at right angles with its fibres, than to tear it by brute force!

In the author's practice a fissure is operated as follows: The sphincter is anesthetized (Figure 5) according to the technic outlined above as in the preparation for the operation of hemorrhoidectomy. The sphincter having been anesthetized and cutaneous anesthesia produced by the injection of one-eighth of one per cent. beta-eucain lactate, the tissues surrounding and beneath the fissure are thoroughly infiltrated with one-half of one per cent. quinin and urea solution.

Figure 15. Wide incision of rectal abcess.

If a sentinel pile is present, this should be thoroughly distended and the distention carried three-quarters of an inch outside of the external extremity of the fissure.

After allowing ten minutes to elapse in order to insure good post-operative anesthesia, the fissure is grasped with pronged forceps and dissected out in such a way that a V-shaped trench-like wound remains, which is twice as deep at the skin surface as it is at the upper extremity. This V-shaped wound if properly made coapts perfectly when the sphincter contracts. When a sentinel pile is present this is of course included in the excision. Any bleeding vessels are twisted and a strip of gauze is placed in the wound and a compression dressing applied.

The patient is allowed to be up and around on the same day, the bowels allowed to move within twenty-four to forty-eight hours, and the after-care consists only in keeping the wound clean, preventing the mucous membrane or skin from growing down into the wound and the cauterization of flabby granulations if any. The whole wound will become agglutinated in two or three days, and requires practically no after-care. White Petrolatum is freely administered to prevent the formation of hard stools during the healing process.

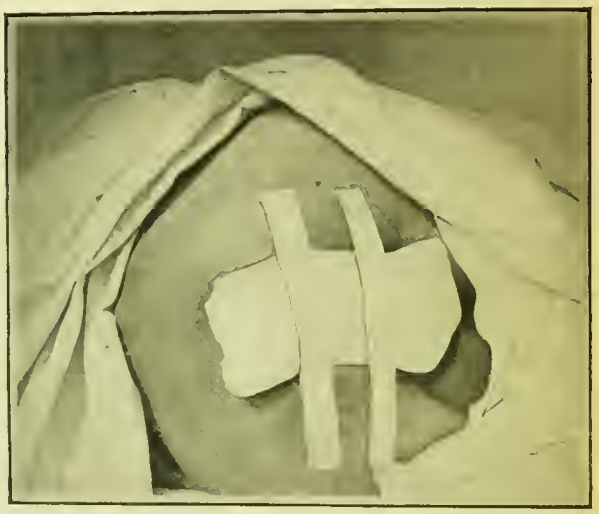


Figure 16. Simple dressing applied after local anesthesia, for rectal operations.

OPERATION FOR ANO-RECTAL FISTULA

Small anal or ano-rectal fistulas, which have been demonstrated by the use of bismuth paste injections and stereoscopic radiographs to be definitely outlined, may be excised by the same technic as that used in the operation for fissure. In order to insure the excision of the whole tract, it is well to again inject the fistula with bismuth paste at the time of the operation in order that any side tracts will not be overlooked. The yellow bismuth paste shows in great contrast to the flesh, and points out little diverticula which otherwise might be overlooked.

If the fistula is a small, direct, complete channel, a piece of annealed silver suture wire,

the ends of which have been made blunt by heating to the melting point (Figure 1 C) is passed through the fistula from without inward, and the inner end drawn out of the anus with a pair of forceps, and twisted around the external end. This twisting threads the fistula on a loop of silver wire, which may also be used as a tractor, drawing the fistula out so that it may be easily excised (Figure 14).

The operation properly finished will leave the fistula dissected out *in toto* threaded on the silver loop. The wound is allowed to heal by granulation and if it is *not packed* but simply drained with gauze, it will heal perfectly. When the sphincter has been completely severed, there will be no incontinence if the sphincter ends are not kept apart by overzealous *packing* with gauze in the after-treatment.

Rather extensive fistulas may be dissected under local anesthesia by the expert proctologist. In the hands of the occasional proctologic surgeon, only the simplest operations should be attempted under local anesthesia, until the technic of local anesthesia in this region is completely mastered.

The operative treatment of many other diseased conditions of this region can be just as successfully performed under local anesthesia as the types of surgical operations described above.

Among these may be mentioned abscesses, (Figure 15), prolapse of the anus or rectum up to the second degree, the removal of polyps, hypertrophied anal papillae, the excision of diseased Morgagnian crypts, the section of hypertrophied rectal valves, the removal of foreign bodies and impactions, Krouse's modification of Balls' operation for pruritus and many others.

The principles to be observed in all surgical operations under local anesthesia are the conservation of the patient's peace of mind, the prevention of unnecessary pain, both operative and post-operative, the lessening of anesthetic shock, prevention of post-operative pneumonia, and nephritis, the shortening of the period of hospital confinement and detention from daily activities, the simplification of surgical technic and detail, the constant reiteration both in precept and in action, that the *patient* is the most *important* thing to be considered in any surgical operation, and the use of local anesthesia teaches the surgeon to perform every operation with the least handling and injury to the tissues. What he is *forced* to do in operating under local anesthesia, he becomes *accustomed* to do under general anesthesia.

The thousands upon thousands of patients who have been successfully treated surgically, under local anesthesia not only in entro-proctology but in other branches of surgery offer the best testimony as to the value, efficacy and success of the use of local anesthesia.

MEMBERSHIP IN AN ASSOCIATION DEVOTED TO YOUR SPECIALTY IS A SINE QUA NON TO SUCCESS. SUCH AFFILIATION NOT ONLY BRINGS THE PLEASURE AND STIMULATION OF PERSONAL CONTACT WITH YOUR CONFRERES BUT ALSO FACILITATES THE INTERCHANGE OF IDEAS AND THE ACCUMULATION OF VITAL KNOWLEDGE. MOREOVER THE ACTIVITY OF YOUR ASSOCIATION IS THE ONLY WAY IN WHICH YOU CAN PROMOTE YOUR STANDING AS A SPECIALIST AND CONSERVE YOUR RIGHTS UNDER EXISTING MEDICAL PRACTICE ACTS.

HERNIA OPERATIONS UNDER LOCAL ANESTHESIA . PRELIMINARY PREPARATIONS . LINE OF INCISION . SUTURES . OPERATIVE METHODS OF CHOICE . TYPES OF CASES . SOLUTIONS AND TECHNIC . INGUINAL, RECURRENT, FEMORAL AND UMBILICAL HERNIA . TOXICITY OF LOCAL ANALGESICS . PROPHYLAXIS AND ANTIDOTES . FURTHER CONSIDERATIONS OF THE OPERATIVE TECHNIC . CONCLUSIONS

BY CHARLES T. SOUTHER, M. D., F. A. C. S. *CINCINNATI, OHIO*

PREVIOUS TO OPERATIONS it is always advisable to have the bowels thoroughly cleaned out, so as to avoid the necessity of stool for two or three days. Care should also be taken to avoid any cutting of the skin of the operative area while shaving. When the patient is a laborer or a man of unclean habits, the body should be specially washed the night preceding operation with soap and water, followed by a ten minutes bath in a tub of clean water containing from 50 to 100 grs. of bichlorid of mercury.

The very free use of alcohol on the operative area, not allowing the excess to run down between the legs, will give good sterilization results. A 5 per cent. solution of iodin may be used locally, provided no water has been used on the skin for several hours previous to its application. Otherwise the pain from the burning of the iodin solution is very disagreeable to the patient. The iodin should be allowed to thoroughly dry before the sterile towels are placed in position. Benzine or gasoline are excellent for sterilization, especially in emergencies, but they should be followed by alcohol, or a painful, burning sensation will follow their use. Alcohol alone answers all purposes in the better class of clean patients. Benzine or iodin alone are equally effective and sufficient if the patient's skin is thoroughly clean.

PRELIMINARY MEDICATION

The following is given by hypodermic injection one hour before operating:

Morphin sulphate,	1-4 gr.
Atropin,	1-150 gr.

Some variation of the dosage may be made on the basis of this quantity for a patient weighing 125 pounds. H-M-C, (Hyoscin, Morphin, Cactoid, Abbott, No. 1), may be used instead of the morphin and atropin and will be found very satisfactory and efficient. Morphin given in this preliminary manner is a very good antidote for cocain poisoning, and is also valuable in counteracting the toxic effects of any overdose of novocain. Personally, I have been fortunate in having no unpleasant toxic after-effects following operations under local anesthesia.

PREPARATION OF THE OPERATING TABLE

It is nothing short of criminal torture to put a patient on a hard steel or glass table with only the usual one-inch thick operating pad to protect him, and expect him to remain quiet during a period of from 30 minutes to 1 hour. We use at St. Mary's Hospital, Cincinnati, a regular operating-table mattress about 5 inches thick and wide enough to allow the arms of the patient to rest on this comfortable, soft pad. The mattress is at least six inches wider than the table and is made of a good quality of curled hair, and for aseptic purposes, is covered with rubber sheeting. It forms a perfectly comfortable bed for fat or thin patients. Only those who have tried it know how such a mattress reduces post-operative backache. In other hospitals, where such a mattress is not available, I supplement the usual thin operat-

ing-table pad with thick pillows, to make a soft, comfortable bed for all cases operated on under local anesthesia. This is an essential point in the success of surgery under local anesthesia and should never be overlooked or omitted. It is also advisable to so adjust the table or pillows that the knees of the patient are slightly flexed and he should be allowed the same head support to which he is accustomed when sleeping. When everything has been done to assure the patient a comfortable and relaxed position the operator is amply repaid by the restful condition of the patient during the entire course of the operative procedure.

FEEDING, LAXATIVES, POST-OPERATIVE VOMITING AND OTHER DETAILS

Patients may have their breakfast on the day of operation, coffee, toast, cereal or any other light food to which they are accustomed, and during the operative procedure many surgeons are accustomed to allow malted milk, tea, water and in some instances *"a smoke."* After operation, except in the presence of complicating nausea or vomiting, a light, nutritious diet is allowed at the usual intervals and continued for 2 or 3 days, until the bowels have been thoroughly moved. Heavier foods are at first avoided in order to prevent straining at stool. Once the bowels have been thoroughly moved, especially in hospital cases, the patient's regular diet may be resumed. Laxatives or purgatives are not used unless an enema fails or gas pains develop, when any of the ordinary drugs or oils for this purpose may be given at the discretion of the operator. Calomel is rather drastic in patients over 40 years of age and it is contraindicated in the presence of pyorrhea or carious teeth, conditions which generally present in middle-aged patients who are subjects for hernia operations.

Post-operative nausea or vomiting is rarely associated with simple cases of hernia or uncomplicated operations; but it may accompany strangulation and cases in which some degree of peritonitis occurs. Under local as well as general anesthesia, post-operative nausea and vomiting is due to causes other than the anesthetic in about 95 per cent. of all cases. While post-operative nausea and vomiting are rare, they may be precipitated by lack of preliminary preparation, excessive trauma, the incidence of peritonitis or too large a preliminary dose of opiates. Rarely is the complication due to overdosage of the local analgesic, although this may accidentally happen.

ILLUSTRATIVE CASE: In one instance severe post-operative vomiting followed the removal of a 27 pound ovarian cyst done under local anesthesia. On investigation, however, it was found that the solution of novocain used had been accidentally *doubled in strength* and more than three times the necessary amount of novocain had been used. Vomiting ceased after 16 hours and there were no other untoward symptoms, the patient making an otherwise uneventful recovery.

In the presence of persistent vomiting it is essential to ascertain the cause which is usually some other than the toxicity of the analgesic. Thorough stomach lavage is indicated in all cases in which vomiting continues for more than 12 hours. Acidosed patients require Fischer's alkaline treatment, followed by alkaline waters, fruit juices and carbohydrate feeding, after nausea has been controlled. Symptomatic treatment avails but little. Persistent nausea or vomiting is a contraindication to the administration of food by the stomach, until nausea has beeen controlled.

THE LINE OF INCISION

The line of incision should always be parallel to the natural folds of the skin, whenever this is possible. Incision for inguinal hernia should follow the folds of the groin and while it should be of ample length to facilitate work, it should not extend into the vascular region of the mons veneris and it should stop at least 1-2 inch short of either end of the anesthetized area.

The incision for femoral hernia should be made parallel to and just below Poupart's ligament or over the greatest bulging of the tumor when the hernia is large. A vertical incision for femoral hernia is not only unnecessary but makes a bad scar and remains tender for a long time. While most text-books and many authorities on the subject respectively illustrate and advocate the vertical incision, my personal experience with the transverse incision has been more satisfactory and

its use can be supported by the best of anatomical reasons. The fact is that transverse incisions are gradually being recognized as superior to vertical incisions in many other fields of surgery.

LIGATIONS, SUTURING AND SUTURES

All vessels encountered in the opening of the hernia wound should be immediately ligated before they are allowed to bleed over the tissues and obscure the anatomy. Consistent ligation of superficial veins and small arteries will prevent the occasional hematoma which forms from the secondary hemorrhage of pinched or twisted vessels. Should a hematoma occur within 4 hours after operation it is advisable to open the wound, secure and ligate the bleeding vessel and close the operative wound without drainage. When found later than this the skin sutures should be removed to provide drainage.

All sutures should be absorbable. I think this is now the consensus of opinion among hernia operators the world over. No. 1, 20 day chromic gut, using a double strand for either a continuous or interrupted suture in coapting the conjoined tendon to Poupart's ligament and also for suturing the external oblique, gives perfect satisfaction. No. 2, 20 day chromic gut may be used when a single strand is desired. Larger or heavier sutures are rarely necessary, although used by many operators. Plain catgut, No. 1, suffices for the superficial fascia and for ligation of the vessels. Kangaroo tendon has many advocates and much merit for coapting the musculature. Horsehair is, I believe, the ideal material for the skin sutures, because if tied too tight it will break. Skin sutures should be so adjusted as to be free from tension. When tied too tight the wound is not only uncomfortably painful, but failure of healing is invited on account of the incidence of sepsis due to tension necrosis. It is very important that the catgut should never be placed in water before being used. This causes it to swell, to grow sleek and to untie very easily, besides breaking the chain of asepsis and inviting infection. Tubes of catgut should be broken and the gut allowed to become rather dry before using to prevent the slipping of the knots. *Three knots should always be made in hernia sutures.* Fine silkworm gut for skin sutures is also desirable. It has many advocates especially for the subcuticular suture. Through and through sutures with silkworm gut, however, are apt to be tied too tight.

The needles used should be full-curved, heavy and blunt. It is hazardous to use a cutting needle in the deep structures. A small, very sharp cutting needle, however, is a great convenience for skin suturing; the so-called boat-shaped, three-cornered, sharp-pointed needle being especially satisfactory in some years of personal use.

The opinions of Coley, Ferguson, Judd and W. T. Bull are certainly worthy of acceptance and these authorities all use catgut in their hernia operations, some chromic, some plain. The majority of operators favor the 20 to 30 day chromic gut, but never larger than No. 2, and Ferguson routinely uses No. 1. Interrupted sutures have the greatest number of advocates.

For lapping the fascia No. 0 chromic gut may be used. A heavier plain or iodin gut has many supporters. It is imperative to emphasize the fact, however, that suppuration constantly presents in all wounds when sutures are tied tight enough to stop the blood supply. *Tissues will become necrotic when strangulated.* It is my opinion that infection and recurrences are due more to tight sutures than to all other causes combined. This is particularly true of skin sutures. Whatever form of non-absorbable skin suture is used, it should be removed from the 5 to the 10 day. If the tissues have been carefully approximated with fine silkworm gut, horsehair, silk or linen, either by the subcuticular or Glover stitch, the suture material will do no harm if left in situ for 10 days. As a rule the skin suture has done all the good one can hope for in about 6 days and union will be more rapid if it is removed at this time.

It is claimed by many that a double strand No. 1 chromic gut is preferable to a heavier suture material used single. The present tendency is toward the smallest possible ligature consistent with the holding power required and the No. 1 chromic gut has proven itself amply satisfactory for most operators. Per-

sonally, I have used nothing heavier than the No. 2 for any kind of work for some years.

In order to tie the knots tightly without strangulating the tissues, make the first knot loose, then insert the point of an artery clamp under the knot and tie the second and third knots as tight as the suture material will permit. On removal of the hemostat the suture will be found tight enough for all operative requirements, but will never be tight enough to strangulate the tissues.

THE OPERATIVE METHODS OF CHOICE

While the writer favors the anatomic operation of Ferguson, he is perfectly willing to accord equal merit to Bassini's method, on account of the large number of operators who favor it. Bull, Coley and others are warm advocates of the Bassini technic. If the hernia operator will closely study Coley's and Ferguson's writings and take the liberty of reading between the lines he will soon realize that these authorities do not differ greatly. Coley calls it Bassini's operation *with or without transplantation of the cord*. Coley's writings have been more especially on hernia in childhood, at which time of life the cure is less difficult.

GENERAL CONSIDERATIONS AND TYPES OF CASES

When we know that about 6 per cent. of all men and over 2 per cent. of all women suffer from some form of hernia, we can realize the importance of being thoroughly familiar with and ready to meet and handle all types of cases. When we also consider that at least 98 per cent. of those afflicted can be cured by an operation that practically has no mortality, we are forced to become interested in the means of keeping this mortality as low as it is and if possible still further reducing it. The remaining 2 per cent. of cases that are difficult or impossible to cure are those in which the following conditions present:

(1) A hernia so old and large that a replacement into the abdominal cavity causes so much increased intra-abdominal pressure that there is graver danger in reducing it than in allowing it to remain herniated. (See W. D. Gatch: Effects of Operation, Posture and Anesthesia on the Circulation: herewith printed in the Year-Book). These cases do not usually strangulate owing to the extreme dilitation of the rings and are troublesome only from the disability they cause and dangerous only from adhesions which may produce obstruction.

(2) A class associated with some heart or kidney lesion or some serious tumor pathology or cancer, in which the hernia is the lesser cause of the patient's disability.

Either of these conditions may be associated with or have produced in the course of their development, a form of hernia known as *sliding hernia,* which is not easy to deal with satisfactorily. During the past five years a number of very excellent articles have appeared on this subject, and they all prove conclusively that expert knowledge and unusual skill are required to successfully operate on this type of hernia.

Strangulated hernia is a surgical emergency and requires early relief or must of necessity prove fatal, if a portion of the lumen of the bowel is included in the constriction. Mortality is in inverse ratio to the length of time elapsing between strangulation and operative relief.

SOLUTIONS FOR AND TECHNIC OF LOCAL ANESTHESIA FOR HERNIA OPERATIONS

While local anesthesia is gradually becoming the anesthetic method of choice in all operations for hernia, its use in the emergency operation for strangulated hernia is an almost imperative necessity and certainly a very vital factor in controlling the post-operative mortality of this operation.

In my personal experience the use of the following solutions has provided safe, efficient and entirely satisfactory local anesthesia for all hernia operations.

Solution No. 1.

Novocain	gr. xx	1.20
Adrenalin (1:1000)	gtt. xv	.90
Normal Salt Solution	oz iv	120.

M-Sterilize by boiling; then add Adrenalin.

Solution No. 2.

Novocain	gr. x	.6
Normal Salt Solution	oz i	30.

M-Sterilize by boiling before use. For nerve blocking only.

Solution No. 3.

Quinin-Urea Hydrochlorid	gr. ii	.012
Aq. dest.	oz i	30.

The following solutions are advised in Percy Shields translation of Braun's masterly work on Local Anesthesia:

Solution No. 1.

Cocain Hydrochlorate	(*or*)	0.1
Novocain		0.25
Normal Salt Solution		100.
Adrenalin (1:1000)		5 drops

Solution No. 2.

Cocain Hydrochlorate	(*or*)	0.1
Novocain		0.25
Normal Salt Solution		50.
Adrenalin (1:1000)		5 drops

Solution No. 3.

Cocain Hydrochlorid	(*or*)	0.05
Novocain		0.10
Normal Salt Solution		10.
Adrenalin (1:1000)		5 drops

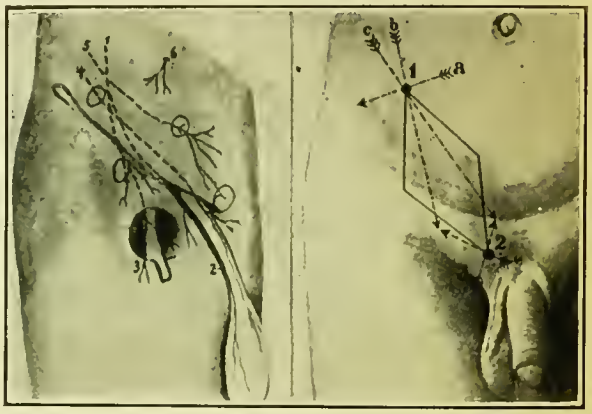
Solution No. 4.

Double the strength of No. 3 by using only 1-2 the quantity of Normal Salt Solution.

The *syringes* required are an ordinary hypodermic syringe with small, fine caliber needles for making the preliminary wheals, thereby producing little or no pain during the initial punctures. For further infiltration a 10 cc. Luer type or any other make of large, all glass syringe is convenient. For the more extensive infiltration the needles should be of larger calibers and from 2 1-2 to 3 1-2 inches in length.

Technic of Infiltration.—After careful preparation of the operative area, outline the following diamond-shaped field for local anesthesia. Four points are selected, one at the anterior superior spine of the ilium, the other at the spine of the pubes, to which is attached Poupart's ligament; another midway between these two points and one inch below Poupart's ligament and the last, midway between the first two points, but 2 inches above Poupart's ligament. This practically encompasses the area which must be obtunded for ordinary inguinal hernias.

A large intercutaneous wheal is infiltrated at each of the four points of the diamond, using about 1-2 drachm of the No. 1 solution. Then the larger syringe is used to infiltrate the base lines connecting these four points. Follow this with a careful infiltration of the external



Figures 1, 2. Relative position of the nerves involved in the operation of inguinal hernia, with small circles indicating the areas infiltrated with novocain (Braun-Shields). (2) Braun's method of introducing local anesthesia into the tissues in preparation of the field of operation, showing the outline of the area to be infiltrated with novocain solution. The base lines are infiltrated and also the deeper structures on the same lines as the skin.

oblique fascia and muscle. This can be done entirely by the sense of touch, aided at times by the index finger invaginated through the ring. This infiltration must be conducted throughout the circumference of the whole area. Next it is advisable to infiltrate the region of the internal oblique muscle where the ilio-inguinal and ilio-hypogastric nerves pass down (Figures 1, 2). Follow this by an effort to infiltrate the region of the anterior crural nerve as it passes out from the pelvic pan under Poupart's ligament external to the femoral artery.

Up to this point about 1 1-2 ounces of the

No. 1 solution will have been used, but this 1 per cent. solution can now be diluted 1-2 with sterile water for the skin incision, thereby reducing the amount of novocain injected. It is very important now to wait about 10 minutes for the obtunding influence of the analgesic to take full effect. The operation can now be proceeded with as if done under a general anesthetic. The skin and superficial fascia are incised and the external oblique exposed. Sharp dissection with a keen knife or scissors is less disturbing to the patient than blunt dissection with the scalpel handle. It is well to remember that the sense of touch is not obliterated by local anesthesia. It is also rather important to thoroughly infiltrate the area around the pubic spine, as occasionally the operative procedure necessitates considerable traction and manipulation in this region. The external oblique should now be opened, well internal to Poupart's ligament, so as to have sufficient tissue to overlap later.

At this point of the procedure the ilio-inguinal nerve can usually be isolated and blocked by an injection of a few drops of the 2 per cent. novocain solution with a very fine needle into the sheath. The operative procedure is now continued according to the requirements of either the Bassini or Ferguson method, or any other technic contemplated.

At this point I wish to call the reader's attention to the cremaster muscle, which forms one of the coverings of the sac, in most cases, and is best described as being tubular in form and containing in its lumen the sac and cord. When this anatomical point is thoroughly understood, the cremaster muscle can be readily opened and disposed of by a longitudinal incision and then wiping it off the cord and sac with gentleness and care. If the infiltration and blocking of the ilio-inguinal nerve has been thoroughly accomplished, the sac can usually be dissected out without pain. Should the patient give evidence of discomfort the tissues about the internal ring may be further infiltrated and also the neck of the sac. This latter procedure is best accomplished after the sac has been opened, at which time, with the finger in the sac as a guide, the neck may be thoroughly injected, after which ligation and fixation of the sac can be accomplished without any pain. The suturing of the internal oblique to Poupart's ligament and the other concluding steps of the technic do not, as a rule, elicit any pain.

As the local anesthesia frequently persists for 1 1-2 hours, even the skin remains sufficiently obtunded to be closed without any further infiltration of the analgesic. If the operative procedure has necessitated considerable trauma, some of Solution No. 3, quinin-urea hydrochlorid, may be injected in the region of the nerve trunks, the neck of the sac and under Poupart's ligament. The experiments of Hertzler have proven rather conclusively that the infiltration of quinin-urea hydrochlorid solution is the best method yet devised for the control of *after-pain,* aside from the use of opiates, which may not only be inadvisable in certain instances, but may precipitate nausea and vomiting. (See A. E. Hertzler: After-Pain and Local Anesthesia: herewith printed in the Year-Book).

This principle of infiltration anesthesia, supplemented by the blocking of all nerve trunks presenting in the field of operation and the obtunding of ligaments, and pedicles, gives perfect satisfaction in operations for direct and oblique inguinal hernias, large femoral hernias and many intra-abdominal operations previously performed exclusively under the influence of general anesthesia.

Patients with any self-control are readily handled under local anesthesia. If placed in a comfortable position on the table and allowed some nourishment during the procedure or water to quench their thirst, and if entertained with music, (See W P. Burdick: The Use of Music During Anesthesia and Analgesia: herewith printed in the Year-Book), or casual conversation by the surgeon, his assistants and the nurses, they withstand even the most tedious hernia operations with a minimum of discomfort and no apparent shock whatever. The conscious patient can materially aid the surgeon by coughing or straining to bring the sac into the wound. It must be remembered that the cord is an exquisitely sensitive structure and any traction on it or the omentum or gut will be resented by the patient, and will invalidate all claims to *painless* operation. While the infiltration of the neck of the sac may obtund a limited area of the peritoneum, even mild degress of traction on this structure may

cause not only pain, but nausea as well. The deft, gentle, painstaking surgeon will succeed with local analgesia when his brilliant, spectacular, slap-dash confrére will fail miserably. Local anesthesia is the handmaiden of the perfected anatomist and surgical technician.

In passing it should be noted that the bladder of all patients coming to operation under local anesthesia should be completely emptied before they are placed on the table, or else the patients may develop a strong desire to urinate during the operative procedure and become very restless. They may even be unable to restrain micturition, thus imperiling all the aseptic precautions of the operation. While urinary retention is an infrequent complication of local anesthesia, it occasionally occurs after obtunding some of the trunk areas, and in such instances catheterization should be employed before the bladder becomes distended. More than one catheterization is seldom necessary unless the bladder is allowed to become enormously distended and thus partially paralyzed.

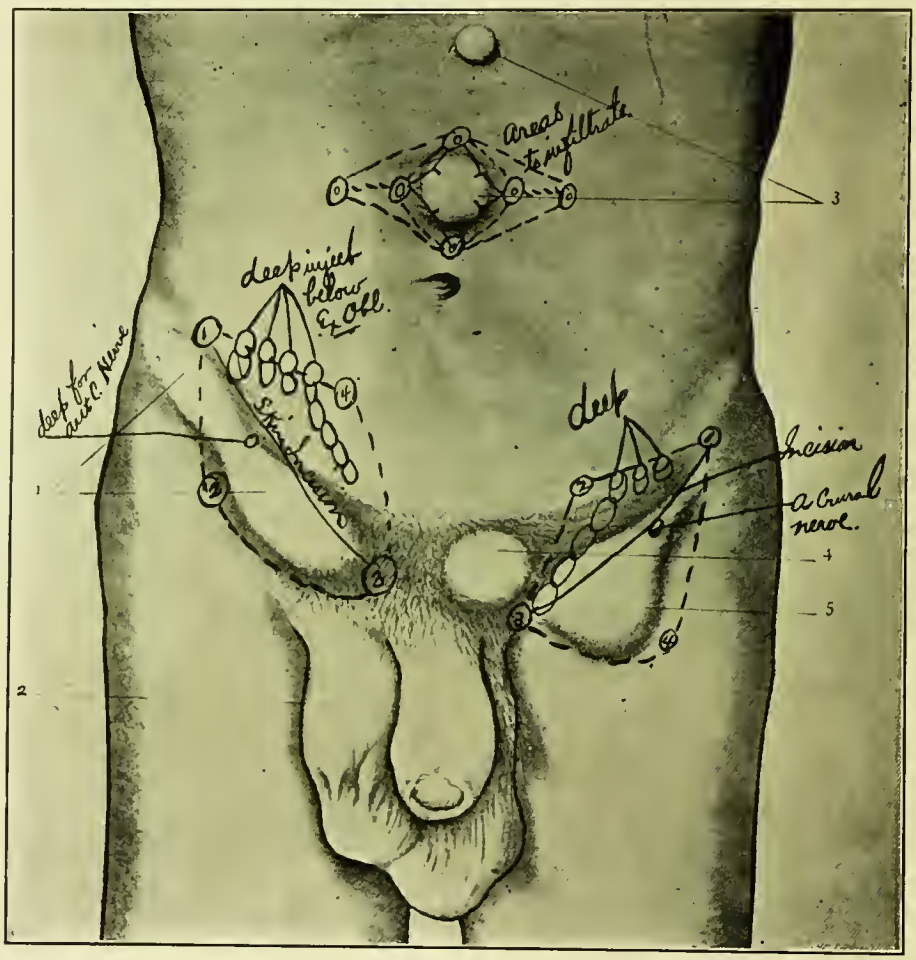


Figure 3. Inguinal, femoral and umbilical hernia. The method of procedure in infiltrating the tissues is illustrated for each form of hernia, and by properly infiltrating the areas indicated, perfect results may be obtained. Infiltration of the anterior crural nerve is only an advantage in femoral hernia.

LOCAL ANESTHESIA FOR RECURRENT HERNIA

Recurrent hernias offer little more difficulty in obtaining successful anesthesia than the or-

dinary forms. It is necessary in recurrent forms to extend the incisions some distance beyond the ends of the old scar in order to expose the nerve trunks above the area of scar tissue. If these nerve trunks can be isolated and properly injected the resulting anesthesia is perfect. These injections into the sheath of the separate nerves is the technic of choice as purely local infiltration is more difficult in the presence of scar tissue from a previous operation. Infiltration may be used after the scar tissue has been excised. The operator, in recurrent hernia is also at the disadvantage of not knowing what method of radical cure has been previously used. In fat subjects Mitchell suggests the dissection of the fat layer surrounding the nerves, after which they may be readily injected.

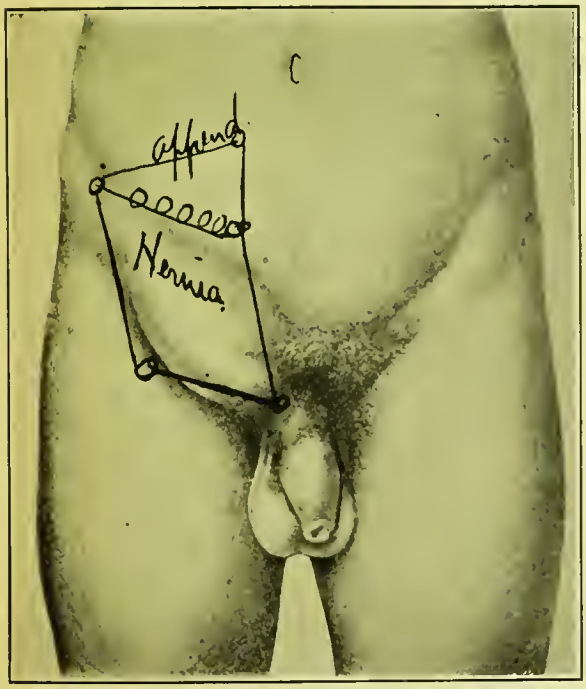


Figure 4. Differentiated areas for infiltration inguinal hernia and appendicitis.

LOCAL ANESTHESIA FOR FEMORAL HERNIA

Some technical details regarding local anesthesia for femoral hernia as well as in the operative technic, must be emphasized. The diffuse infiltration, as suggested by Braun, and so satisfactory in inguinal hernia, is equally advantageous for femoral hernia, although it should always be supplemented by a separate skin injection along the line of the incision, just below and parallel to Poupart's ligament. As the femoral vein lies in close apposition to the hernia, care should be exercised not to injure it during the infiltration or to inject the solution into the venous circulation. The needle is also carried through the external oblique above Poupart's ligament and a diffuse injection made beneath this muscle to block the fibers of the ilio-hypogastric and ilio-inguinal nerves, which descend into the femoral region. Usually there is no difficulty in freely dissecting the sac, after which its neck should be injected and the injection carried well up into the femoral ring in order to insure a painless high ligation of the sac. The contents of the sac may be handled according to the surgical indications. Resections of the intestines can be done painlessly, if the mesentery is not dragged upon. Usually, after ligation, the

Figure 5. Dissection to show the extent to which the local anesthesia is operative, and to show the location of the incision in the aponeurosis of the external oblique, leaving the external ring intact as a landmark. Cord coming out through the external ring. Separation of fibers of the external oblique beginning above.

lower portion of the sac is removed and the stump is allowed to retract within the femoral ring. As the closure of the femoral ring involves no sensitive structures, the required sutures can be placed with absolute freedom.

LOCAL ANESTHESIA FOR UMBILICAL HERNIA

It is interesting to note that many operators are now performing the radical cure of the most extensive umbilical hernias as well as the largest lipectomics under local anesthesia. Peculiarly fat subjects are poor subjects for general anesthesia and these patients may be much more satisfactorily handled by using local anesthesia.

The nerve supply of the umbilical region does not lend itself to regional analgesia or the injection of separate nerve trunks and consequently the diffuse injection with a low percentage solution of the analgesic is indicated. The double elliptical line of skin incision is injected specially, and the long, large caliber needle is carried down along the side of the hernia to the musculature and the entire region of the hernial protusion is bathed in the weak, analgesic solution. It is important when dissecting through the layer of fat to inject the larger vessels or more prominent nerve fibers as they present. Each large vessel carries a nerve filament and unless it is obtunded sharp pain will result if the vessel is cut and persist if the vessel is ligated. When the muscle is reached it is advisable to carry the dissection as close to the neck of the sac as possible.

Once the sac has been thoroughly isolated the needle is introduced into the sac wall and the entire circumference of the neck of the sac injected with the analgesic solution, extending the injection into the peritoneum as far as the previous dissection permits. This allows the sac to be cut off flush with the muscle. In doing the Mayo operation it is important at this stage to introduce the needle through the muscle and to thoroughly inject the subserous connective tissue, to obtund the area for placing the internal sutures. Local anesthesia for large umbilical hernias requires a very considerable amount of the analgesic solution and consequently it is imperative to use the lowest percentage solution compatible with desensitizing the tissues, or else an overdose of the analgesic agent may result.

LOCAL ANESTHESIA FOR POST-OPERATIVE HERNIAS

The dissection of the muscle layers, in post-operative hernias, is the difficult, painful and tedious part of these troublesome operations, and it is vital to the success of the anesthesia and operation to painstakingly infiltrate the muscular tissues with an abundance of the analgesic solution. Further, the successful handling of post-operative hernias depends on the skill of the operator is being able to accurately dissect out the various muscular layers to provide adequate overlapping flaps.

TOXICITY OF ANALGESICS, PROPHYLAXIS AND ANTIDOTES

In relation to the toxicity of local anesthetic agents, it is my experience that solutions as weak as 2 grains to the ounce are efficient for all purposes in hernia operations, and yet I have had no untoward experiences when as much as 15 grains of novocain were used during one extensive and prolonged operation. Care should be exercised in limiting the amount of adrenalin injected as systemic complications are more apt to arise from this circulatory disturber than from the novocain itself. Morphin and atropin as a preliminary is a good prophylactic measure against the incidence of toxicity or circulatory disturbances due to tension, fear or emotional shock. Should toxic symptoms arise, indicated by sweating, pallor, restlessness, hurried breathing and nausea, the immediate antidote is the Engstad Method of administering ether by the drop method to the point of securing its stimulating, not its analgesic or anesthetic effect. A few whiffs of ether, given with a large admixture of air will immediately stabilize the circulation and restore normal respiration. Toxic symptoms may be precipitated by sudden hemorrhage, on account of which the sum total of the analgesic agent in the tissues rises in direct proportion to the blood lost. In such instances the intramuscular injection of 1 cc. pitutrin will have

an almost instantaneous effect, and this may be followed by intravenous saline or colloidal gelatin and saline.

SOME FURTHER CONSIDERATIONS OF THE OPERATIVE TECHNIC

The fact that one book on hernia describes 45 methods for the operative cure of inguinal hernia and 27 methods for the cure of femoral hernia, means that many men are seeking to have their names applied to their operation or there is some fault to find with most if not all the methods yet devised. I am inclined to believe, after an exhaustive study of the subject, that it is a case of *"straining at a gnat and swallowing a camel!"*

Proper application of the best known surgical principles to the cure of hernia will result in success and the radical cure of 98 per cent. of all cases operated on. This paper is based on 10 year's special study of hernia, from text-books, cadaver dissections, visits to the clinics specializing in the technic, work among my colleagues and personal operative experience. I was willing very early in my career to concede that scientific operative work for the cure of hernia was much less common than it should be and that the radical cure of hernia was one of the difficult major operations when considered from all its standpoints. This is self-evident from the face of the well-established fact that until the last 10 years, recurrence varied from 5 to 20 per cent. in the hands of various operators, while at present 98 per cent. of cures follow good work.

The student of the surgical technic of hernia operations must have such a perfect knowledge of the normal anatomy of the hernia region as to be able to demonstrate it on both the cadaver and the living subject. Also, it is essential to be able to recognize this same anatomy when the parts are distorted by the many pathological conditions found in hernia. I do not undervalue the teaching force of artistic drawings, but I also believe that more photographs of the actual conditions found, both in text-books and articles, would impart to under and post-graduate students the knowledge of the pathology and anatomy as it is actually found at operation, and would thus enable them to identify it more accurately, and thereby improve their technical skill in performing any contemplated operation in a thoroughly scientific manner. The prevalence of hernia and the fact that the condition is curable in 98 per cent. of all cases, shows the vital necessity of teaching the proper surgical technics for its cure. Few graduates or even internes have a competent surgical knowledge of hernia and it is imperative for the man who expects to perform the operation to study it as an assistant to some surgeon capable of doing the operations in a masterly manner. The simple relief of strangulated hernia as an emergency operation is no criterion of an operator's skill in the routine procedures.

Incision for hernia includes (1) the incision through the skin, fat and superficial fascia, and (2) the aponeurosis of the external oblique. Skin and fat should preferably be lifted up and either cut with a scissors or transfixed with a pointed knife, so as not to wound the aponeurosis of the external oblique at a point that is not desirable. Wm. Mayo often makes the assertion, in his teaching, that skin and fat are only coverings and are limited only by the contents within. These tissues, consequently, have no retentive or curative influence in the operation for hernia.

The incision in the external oblique muscle or aponeurosis can be made from below up or from above down, (Bodine and Judd), and far enough from Poupart's ligament to allow of whatever amount of overlapping may be indicated in a given case. The rule is to divide this aponeurosis half way between Poupart's ligament and the rectus muscle or linea semilunaris; the external ring can be left intact. This overlapping causes the strain to be taken off the internal oblique sutures and allows more perfect union with the internal oblique and the deeper structures of the canal, meaning the cord, transversalis fascia and peritoneum.

Skin and fascia are reflected below Poupart's ligament and above the linea semilunaris, giving full view of the entire hernia region and greatly facilitating the identification of anatomical structures, making the operation easier and more quickly accomplished. It also shows the location of the incision, or rather the point at which the fibers of the aponeurosis of the external oblique are sepa-

rated, beginning above and going down to the semi-circular fibers that form the external ring. These ring fibers may or may not be cut, or they may be stretched out and nearly obliterated in large scrotal hernias. In a small hernia don't cut the fibers; in large hernia it is better to cut and overlap for support.

If we leave a large leaf in the lower flap of the external oblique aponeurosis, we can grasp

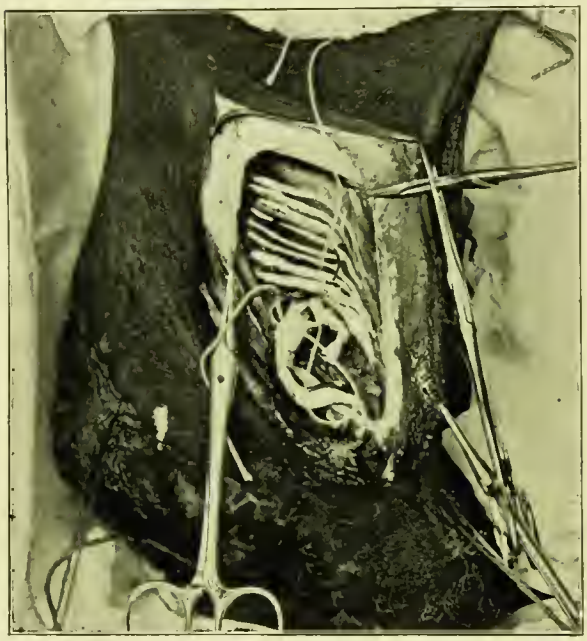


Figure 6. Showing external oblique incision; direction of muscle fibers of internal oblique, sac with neck ligated and being transfixed; cord, deep epigastric vessels and outer pillar of external ring may be seen in their normal relation to each other.

it with small forceps or rubber-covered clamps and with gauze wipe off the under surface of the aponeurosis and expose, without effort, the shelving edge of Poupart's ligament, which is an early and important step in both the Bassini and Ferguson operation.

This usually takes us down to the cord and the sac in a small hernia will usually be found above and slightly internal to the cord. That is, the sac is next to the conjoined tendon and the cord is next to the shelving edge of Poupart's ligament, both structures usually receiving a covering from the cremaster muscle.

The relative retentive power and influence of the cremaster muscle in the radical cure of hernia depends on (1) the method of operation and (2) on the size and development of the muscle itself. The cremaster forms, with the fascia, one of the coverings of the sac while it passes through the inguinal canal. By opening this sac and carefully preserving the cremaster muscle it can be used to cover over the cord and attach to the underside of the conjoined tendon and the internal oblique, (Halstead). In this method it forms the first step in the suture part of the operation.

It is impracticable to use the cremaster muscle in the Bassini operation or in cases where the muscle is deficient in development and has little or no retentive power. The importance given to this muscle by Halstead and Ferguson and others has established its use as a definite detail in the operative technic.

Figure 6 is illustrative of what seems to me an advantage in placing the sutures holding the internal oblique (conjoined tendon) over to Poupart's ligament. These sutures are placed as mattress sutures, beginning by passing the round-pointed half-curved needle from without through the external oblique above Poupart's ligament on the outer flap, while the same is held upon the finger, then from without this internal oblique, coming out through the lower flap of aponeurosis of the external oblique fascia, so that when tied the knot is external to the external oblique and no knots are left in the canal.

OVERLAPPING THE EXTERNAL OBLIQUE FASCIA

This can always be done, provided the primary incision is placed midway between Poupart's ligament and the linea semilunaris. When the external oblique fascia is overlapped (Figures 7 and 8), it takes up the surplus in the tissues and by putting more tension on the fascia causes the linea semilunaris to be drawn nearer Poupart's ligament, relieving tension on the internal oblique and conjoined tendon, thereby facilitating the union of the deeper structures. This carries out the most accepted principles advocated by the best surgical authorities in the treatment of all ventral hernia, namely the overlapping of the fascia.

DISPOSITION OF THE SAC

When we realize that hernia is cured by the obliteration of the sac alone, either surgically, by the injection of various substances or mechanically by the use of some device for simply retaining the sac or contents within the peritoneal cavity, then we can realize the importance of this phase of the technic.

A careful perusal of what W. B. De-

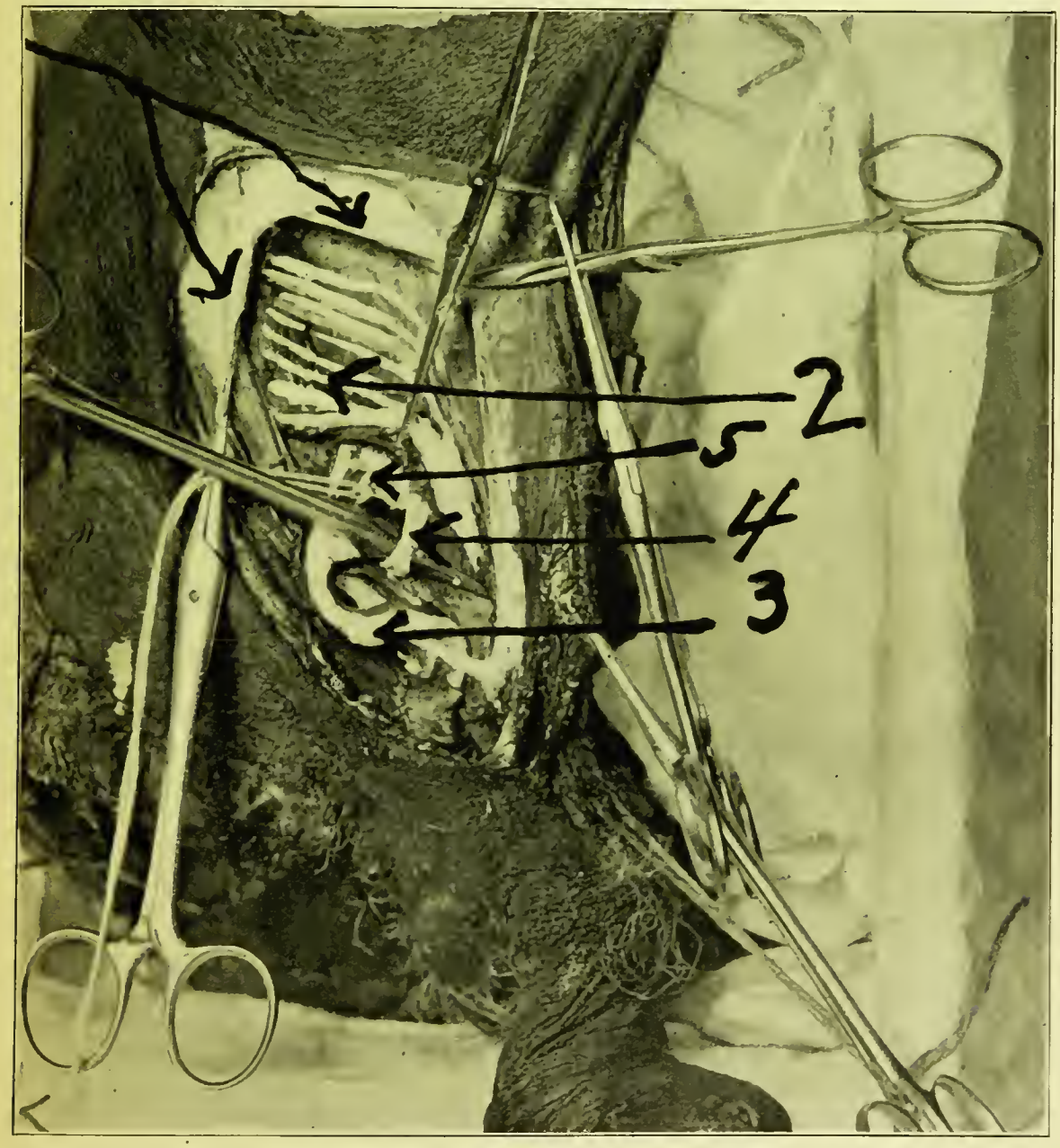


Figure 7. Showing important anatomical structures in hernia. (1) Double arrow, external oblique reflected; (2) internal oblique; (3) cord; (4) deep epigastric vessels; (5) neck of sac ligated, ready to be transfixed. White lines on the internal oblique show the direction of the muscle fibers. Local anesthesia in no way interferes with the proper identification of the various tissues.

Garmo, H. O. Marcy and A. H. Ferguson have written on this point of the technic, would lead one to believe that the last word has been said on the subject.

Deanesley, (British Medical Journal, June 17, 1905,) believes that an operation that effectually removes the sac is followed by 95 per cent. of cures.

Bull and Coley, (Medical Record, March 18, 1905,) report 1,500 operations for the

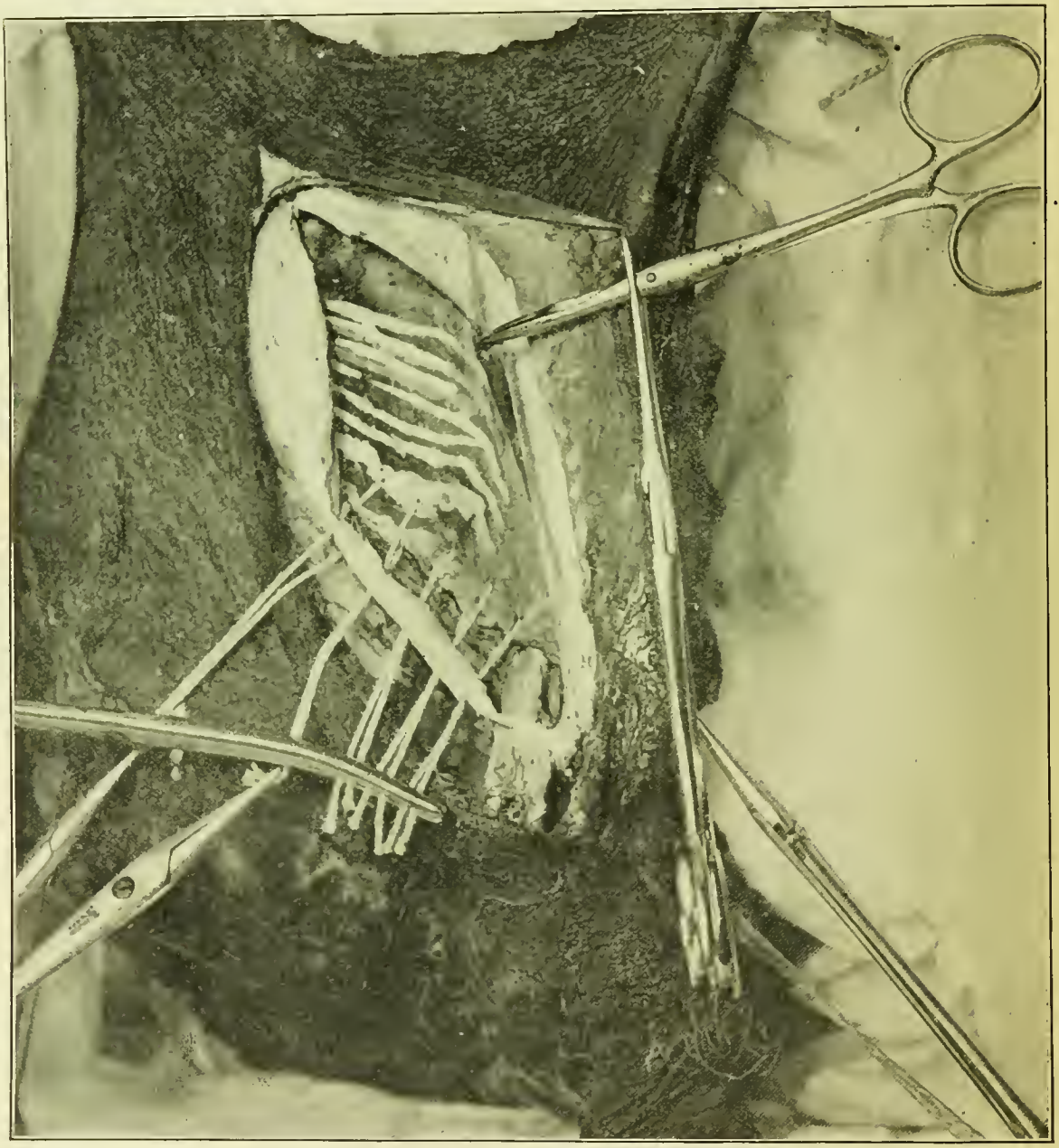


Figure 8. Showing five interrupted sutures passed through the internal oblique and conjoined tendon, one end under the shelving edge of Poupart's ligament, with the other passed through the external oblique fascia, so as to tie all knots above the external oblique fascia and leave no knots in the canal. Modified Ferguson operation. (Photographs have been used to illustrate structures as they appear during operation.)

radical cure of hernia, all but 21 patients being under 14 years of age. Mortaliy 0.3 per cent.; 6 relapses in 1,076 cases, and 5 relapses in 125 cases where the cord was not transplanted.

Ricketts, (American Medicine, May 4, 1901,) collected 6,026 cases; average recurrence in hands of 34 operators was 5.58 per cent.

A. H. Ferguson collected 4,257 cases operated on by the Bassini method, with 5.31 per cent. recurrences. He also states that by his typic method, out of 356 cases operated on, he was able to trace 225 cases with no recurrences.

Figure 9. Showing the internal oblique and conjoined tendon, held by five sutures to Poupart's ligament. Operation complete, except for closure of fat and skin, all knots tied above the external oblique muscle, and fascia overlapped.

Galeazzi has collected 1,334 cases by Bassini's method, with 216 per cent. recurrences.

Later, Bull and Coley, (Journal American Medical Association,) report on 2,100 personal cases with only 2 per cent. plus returns, practically all by Bassini's method—that is simple dissection of the sac, ligation, amputation and replacement below the internal oblique.

Macewen dissects the sac free, opens it and inspects it; if large it is partially removed, then folded on itself and used as a boss behind, internal to or under the internal oblique. The closed or folded sac is caught by medium chromic catgut and a non-cutting needle; the needle being passed from within out through the transversalis fascia, internal and external oblique; then the opposite end of the thread is passed the same way, making a mattress suture, which when tied, holds the sac so that it can no longer make any pressure on the previous site of the hernial opening.

This same disposition of the sac is advised in Ferguson's description of Halstead's method. The sac is transfixed by mattress suture through the muscle from within out and tied.

Lanphear also anchor's the sac.

Roswell Park makes use of the sac as McArthur does the aponeurosis of the external oblique and sutures the muscles together.

Sellenings, (American Journal of Surgery, March, 1909,) publishes a new operation for inguinal hernia, which consists of treating the sac as it lies in its bed undisturbed by putting in from the peritoneal side, after the sac has been opened and irritated by gauze or needle scarifying, a purse-string suture is used at the neck; a second series of interrupted purse-string sutures are put in and tied so as to obliterate the sac cavity, without disturbing its bed, finally closing the incised edge with a continuous suture. The rest of the operation is done according to the technic of Ferguson and Bassini. Sellenings claims to have derived his idea from Matas' operation for aneurism and offers proof of the transformation of the peritoneum into fibrous tissue, showing that a serous cavity can be completely obliterated by proper approximation sutures and disuse. This has been very conclusively proven without operation. The truss does it in the young and the injection of irritating fluids occasionally accomplishes the same end in the adult.

Ochsner has called attention to the fact that after the removal of the sac the round hernial openings will close without further treatment. He makes use of this fact in his technic for femoral hernia, but it only holds good where the opening is small and the muscle has a chance to return to the normal position and cover the opening. We must ultimately rely

on the overlapping of the fascia in all ventral hernias after the sac has been thoroughly dissected out and separated from the fascia and all superfluous tissue removed.

E. K. Herring advises an operation for hernia in children in which he does nothing but treat the sac by opening it wide, circumscribing the peritoneal coat and coapting the peritoneal edges, allowing the sac to remain in the canal, which is simply closed by suturing the skin. Muscle sutures are used only when the child has a cough. This procedure, he claims, cures 95 per cent. of all children operated on by the method.

A. C. Butler treats the sac in inguinal hernia as Ochsner does in femoral. Most all the 27 methods for femoral hernia, the 41 methods for inguinal and the 15 methods for umbilical hernia, reported by Ferguson, dispose of the sac by dissection, ligation and amputation, and with that the treatment of the sac ends.

Kocher's method is rather unique in that he does not open the external oblique except over the internal ring, and then after dissecting up the sac, he passes a forcep through the opening of the external oblique and grasping the sac, draws it out through the opening, twists the sac on itself and stitches it on top of the external oblique. This original method was later modified by the removal of the sac, as if it was followed, according to Ferguson, by 20 per cent. of recurrences.

In looking over the large number of methods we can see the gradual elimination of the many in favor of the few, and those few are the methods by which most of the radical cures of hernia are done to-day. The methods of Bassini, Macewen, Ferguson, Butler, Halstead, and Ochsner, (femoral), are based on surgical principles, but few operators follow strictly any one method. They simply apply surgical principles to the conditions found at operation.

All authorities agree on the obliteration of the sac and most of them on its removal. One surgical and mechanical principle which we must respect is that in removing or obliterating the sac we must also remove the protusion of peritoneum or the infundibuliform process of peritoneum, which constitutes the sac stump, and leave no pocket at its former site, which will assist in directing the intra-abdominal pressure to one point. Hence the philosophy of using the methods of Macewen, Halstead, Butler, or Lanphear. This rule applies to all forms of hernia and is best accomplished by removing the sac and anchoring the stump so that future pressure is directed to a point away from the original site of the hernia.

The foregoing also applies to congenital hernia. Congenital hernia in the male means that the contents of the sac extend to the testicle, that the tunica vaginalis testis forms part of the sac and is continuous with it, and that the infundibuliform process has never closed to make a normal tunica vaginalis testis. In so far as the treatment of the stump of the sac is concerned, the sac cannot be completely removed in congenital hernia without removing the testicle, hence the sac should be opened, left in place, divided near the neck and the proximal or abdominal end closed, either by over-and-over sutures, or ligated and the stump treated as previously indicated. The distal end of the sac can be treated after the method of Sellenings, or everted as in the Doyen method of operating for hydrocele, which causes complete obliteration of the tunica vaginalis testis and prevents the occurrence of hydrocele subsequently.

Resection of intestines and excision of incarcerated omentum are at times necessary in strangulated forms of hernia. When these complications present, they can be handled as readily under local as general anesthesia, providing traction is obviated. An efficient method of testing the circulation in an apparently strangulated portion of bowel, is to replace the doubtful piece of gut into the cavity, having first passed a long, heavy suture through the mesentery under the gut, so that the same section of bowel may be reinspected before closing the hernia. This relief of tension is frequently followed by a return of the color and normal circulation. When the gut cannot be replaced without undue pressure, it is best to enlarge the ring, or make a second opening above and pull the gut back within the cavity, especially in femoral hernia. It is interesting to note that the sac in femoral hernia may be removed through an ordinary abdominal wound, in many cases.

C. H. Frazier, of Philadelphia, (Annals of Surgery, October, 1911, 555), shows the only

cut I have ever seen illustrating the mattress suture for the internal oblique and Poupart's ligament and external aponeurosis, which advocates the tying of the sutures all external to the external oblique. Rose and Carless, (Manual of Surgery, 1907,) illustrate Frazier technical point, but no emphasis is put on it in the text.

CONCLUSIONS

In conclusion it may be stated that:

(1) Local anesthesia for hernia operations is not the anesthetic of choice for the amateur.

(2) With proper knowledge of the regional anatomy, the technic of nerve blocking and infiltration, any of the classical operations for hernia may be successfully completed under local anesthesia.

(3) The type of operation is entirely at the discretion of the operator, the same as under general anesthesia.

(4) Extreme gentleness in handling the tissues is one of the prime requisites for success in operating under local anesthesia.

(5) The ilio-inquinal branches of the ilio-hypogastric nerve are readily identified and need not be cut when proper dissections are made.

(6) Tension on sutures should never exceed that necessary for approximation of the tissues involved.

(7) Every possible detail regarding the comfort of the patient under operation should be routinely utilized.

(8) Recurrences depend in some measure on the cutting of nerve-trunks, so these should be scrupuously conserved in all hernia operations.

THE GLOW WORM IS THE ENEMY OF THE SNAIL BECAUSE IT SUBSISTS UPON THE SNAIL. THE METHOD OF ATTACK IS BY BITING SOME EXTENDED PART OF THE SNAIL AND CAUSING IT TO BECOME INSTANTLY ANESTHETIZED. IF SEVERAL GLOW WORMS PARTAKE OF THE SNAIL IT WILL DIE; BUT IF ONLY ONE GLOW WORM DOES SO, THE SNAIL WILL RESUSCITATE ITSELF ON THE FIFTH DAY, OR IF IMMERSED IN NORMAL SALT SOLUTION, IT WILL RESUSCITATE ON THE THIRD DAY AND CONTINUE TO LIVE. THE WASP IS THE DEADLY ENEMY OF THE SPIDER BECAUSE THE SPIDER IS TO BECOME THE FOOD UPON WHICH THE YOUNG WASPS SUBSIST. THE WASP STINGS THE SPIDER IN THE THORACIC GANGLION, WHEREUPON THE SPIDER BECOMES IMMEDIATELY PARALYZED AND IS CARRIED AWAY TO THE MUD DOBER'S NEST AND THE WASP'S EGGS ARE DEPOSITED UPON THE SPIDER WHERE THEY REMAIN UNTIL HATCHED. THE PARALYZED SPIDER REMAINS ALIVE DURING THE PERIOD OF INCUBATION SO THAT THE YOUNG WASPS MAY HAVE LIVING FOOD TO SUBSIST UPON. IN THE CASE OF THE SNAIL AND THE GLOW WORM IS FOUND INSTANT AND COMPLETE ANESTHESIA; WHILE IN THAT OF THE WASP AND SPIDER IS TO BE FOUND INSTANT, COMPLETE AND PERMANENT PARALYSIS, EACH OF WHICH IS MORE PERFECT THAN ANY KNOWN ARTIFICIAL MEANS.

—Benjamin Merrill Ricketts.

PROSTATECTOMY UNDER LOCAL ANESTHESIA . GENERAL CONSIDERATIONS . THE CONTROL OF SHOCK . DANGERS PECULIAR TO PROSTATICS . PRELIMINARY CYSTOTOMY . FUNCTIONAL KIDNEY TESTS . TECHNIC FOR SUPRAPUBIC CYSTOTOMY . INTRAVESICAL ANESTHESIA . PREPARATORY MEDICATION . TECHNIC OF THE SECOND STAGE OPERATION . MICULICZ PACK FOR HEMORRHAGES . ADVANTAGES

BY CARROLL W ALLEN, M. D., F A. C. S. *NEW ORLEANS, LA.*

IN PRESENTING A PAPER on a subject as important as *Prostatectomy,* there are many facts which at times may be of vital importance which do not deal with the technical performance of the operation, or with the details of anesthesia, and yet which are little understood and often omitted in the practice of many fairly competent men. A thorough knowledge of these essentials with the judgment necessary for their application often distinguishes the surgeon from the operator.

GENERAL CONSIDERATIONS

My discussion of these details is due to the appreciation of their importance as their omission may lead to error and bring to discredit a method which I am convinced has much to commend it.

One factor of great importance is the age of these patients, as most of the cases requiring surgical relief for this condition have reached or passed middle age, and many of them are infirm or weakened by suffering and infection. In the old and feeble, prostatectomy is a formidable operation, though not attended by a greater mortality than that following any other major operation in the same class of patients. However, it may even show a more favorable comparison by observing certain methods in the handling of these cases.

The method which I wish to present is the result of a process of gradual evolution and improvement in handling these patients. Beginning with the *two-stage* operation and the adoption of the *anoci-association* principles to control shock, and the logical addition of adrenalin for the control of hemorrhage, it has gradually progressed to the point of complete elimination of all general anesthetics, which are now never necessary, but which, however, should be preferred in undoubted malignancy of the prostate in which methods of infiltration should be avoided.

THE CONTROL OF SHOCK

The particular advantage claimed for local anesthesia in this field is the avoidance of all shock. The two great factors in the production of shock are *trauma and hemorrhage,* and to these, in the great majority of surgical procedures, is added the toxhemia of the general anesthetic. In the recent and more improved methods of general anesthesia toxhemia may be practically eliminated as a shock-producing factor, yet general anesthesia, nevertheless, has its dangers in the deranged stomach, possible pulmonary and, particularly in prostatectomy, renal complications.

DANGERS PECULIAR TO PROSTATICS AND PROSTATECTOMY

These cases present another danger fully as great as any of the above which I believe is responsible for a large proportion of the mortality in these patients, a danger peculiar to these cases.

Few persons requiring prostatectomy present themselves for operation before they have seriously felt the inconvenience of this condition; many have probably already been initiated into catheter life; some have had one or more attacks of acute retention of urine from prostatic congestion, and practically all will show considerable residual urine and possibly some renal complications; nearly all are disturbed frequently at night by having to arise to urinate. The kidneys have gradually accustomed themselves to this condition and are working against considerable back pressure, and the sudden relief of this pressure at operation completely upsets the renal equilibrium leading to congestion with diminished excretion, or probably anuria. *Here lies the particular danger in these cases, and to avoid it we must first relieve the bladder and permit the kidneys to recover by performing these operations in at least two stages in all cases that show much residual urine or are suffering from retention at the time of operation. The danger, too, of suddenly relieving a distended bladder in these cases cannot be overestimated; vesical hemorrhage may occur, associated with renal suppression. In my observation, this procedure alone has caused as great a mortality as prostatectomy.*

In extreme cases such bladders should never be opened at once, unless badly infected and the danger of general infection too great for delay. They should be gradually evacuated by catheter, removing but a portion of the urine at a time, at two or three-hour intervals, or if almost completely emptied one-fourth to one-third as much boric acid solution reinjected as there was urine removed. This gradual emptying process should consume from twenty-four to forty-eight hours before the bladder is opened.

PRELIMINARY CYSTOTOMY

Rarely a case is met with in which there is considerable distention and the passage of a catheter too painful, difficult, or even impossible of accomplishment. In such cases, if the suprapubic incision is carried down to the bladder, the bladder can then be emptied by a gradual process of aspiration at intervals of several hours, gradually withdrawing more and more at each successive aspiration, thus overcoming the difficulty. During these intervals the suprapubic wound is kept packed. After twenty-four or forty-eight hours the bladder, which is now fairly collapsed can be opened with safety.

The method of performing the cystotomy and of dealing with the bladder afterwards is of some consequence. It may be opened with a free incision with the introduction of a tube or catheter to its base and the attachment of some syphoning apparatus, or the escape of urine may be effectively controlled by making a small buttonhole opening into which is passed a Pesser Catheter. The incision is then infolded and held by two stitches, one placed on either side of the catheter. Such a valve-like closure will leak very little, if at all.

The advantage of this last method is quite apparent, as it permits the collection of all urine and in this way the functional activity of the kindneys can be accurately gauged. It will usually be found that the urinary excretion for the first two days diminishes considerably following the cystotomy, gradually increasing from the third to the fifth day, and is about normal by the end of the first week. By this time, if the patient's general condition is good as shown by normal appetite with good digestion, free bowel movements and after a few nights' normal restful sleep, free from the annoyance of frequent urinations, the removal of the prostate can be undertaken. It is usually noticed that the prostate diminishes decidedly in size following the cystotomy due to the relief of the congestion and this diminution in size facilitates its later removal.

FUNCTIONAL KIDNEY TESTS

If any question exists regarding the condition of the kidneys a further delay is necessary or their capacity may be tested by phenol-sulphonephthalein, and under no conditions should the prostatectomy be attempted until they have reached a fairly normal condition of elimination. By handling patients in this way many bad risks and feeble individuals may be safely carried through the surgical ordeal.

During the interval between the suprapubic

cystotomy and the prostatectomy the bladder should be washed once or more daily with warm boracic solution and the suprapubic wound kept lightly packed, and any infection in the cellular planes which may have occurred, which, however, is rare, should be well under control before the final operation is attempted.

symptoms yet seem much depressed with loss of weight and poor appetite. Such cases should not have the final stage of the operation completed until they have fully regained their normal and show improvement in weight and appetite.

Nothing improves these cases more than

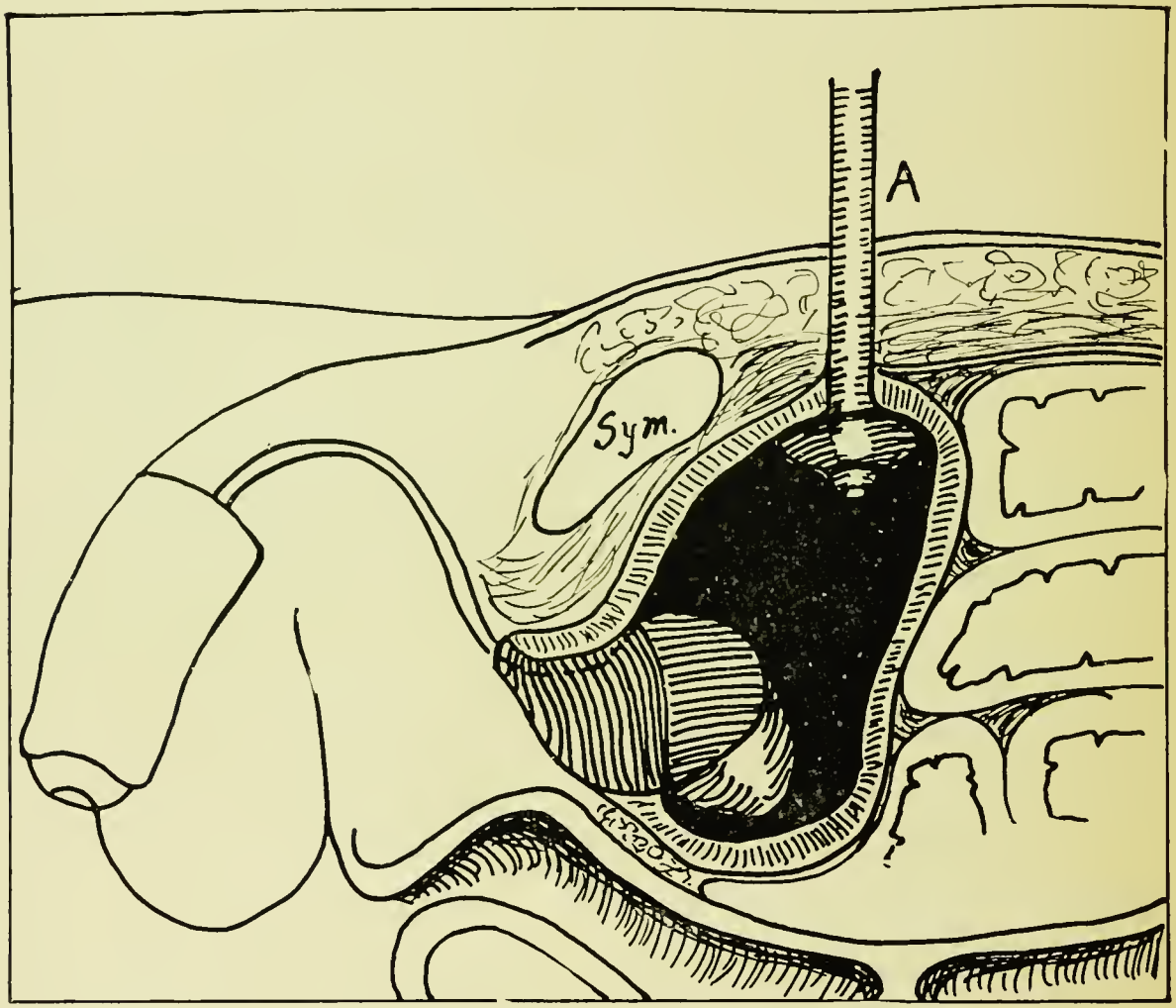


Figure 1. A preliminary cystotomy with the Pesser catheter in position and the cystotomy incision and layers of the abdominal wall sutured to make a water-tight wound. This technic provides an ideal operative field for the second stage operation.

IMPROVING POOR SURGICAL RISKS

Occasionally a case is met with in which the kidneys seem to have recovered their normal equilibrium as shown by the output of urine, and the patient relieved of all vesical

frequent tub baths. There is no danger of harming the bladder or infecting it by complete immersion, but it is usually best to give the bladder irrigation following the bath. If the patient is too feeble to walk he is gotten out in a rolling chair and kept in the fresh air and sunshine as much as possible; when

he is able to be on his feet some form of urinal is used to keep him dry and he is encouraged to get about as much as possible. Unless the kidneys have been badly damaged by ascending infection or other complications exist, is first irrigated freely through a catheter with boracic acid solution and left moderately distended.

It is better to complete the infiltration of the entire field of operation before making the in-

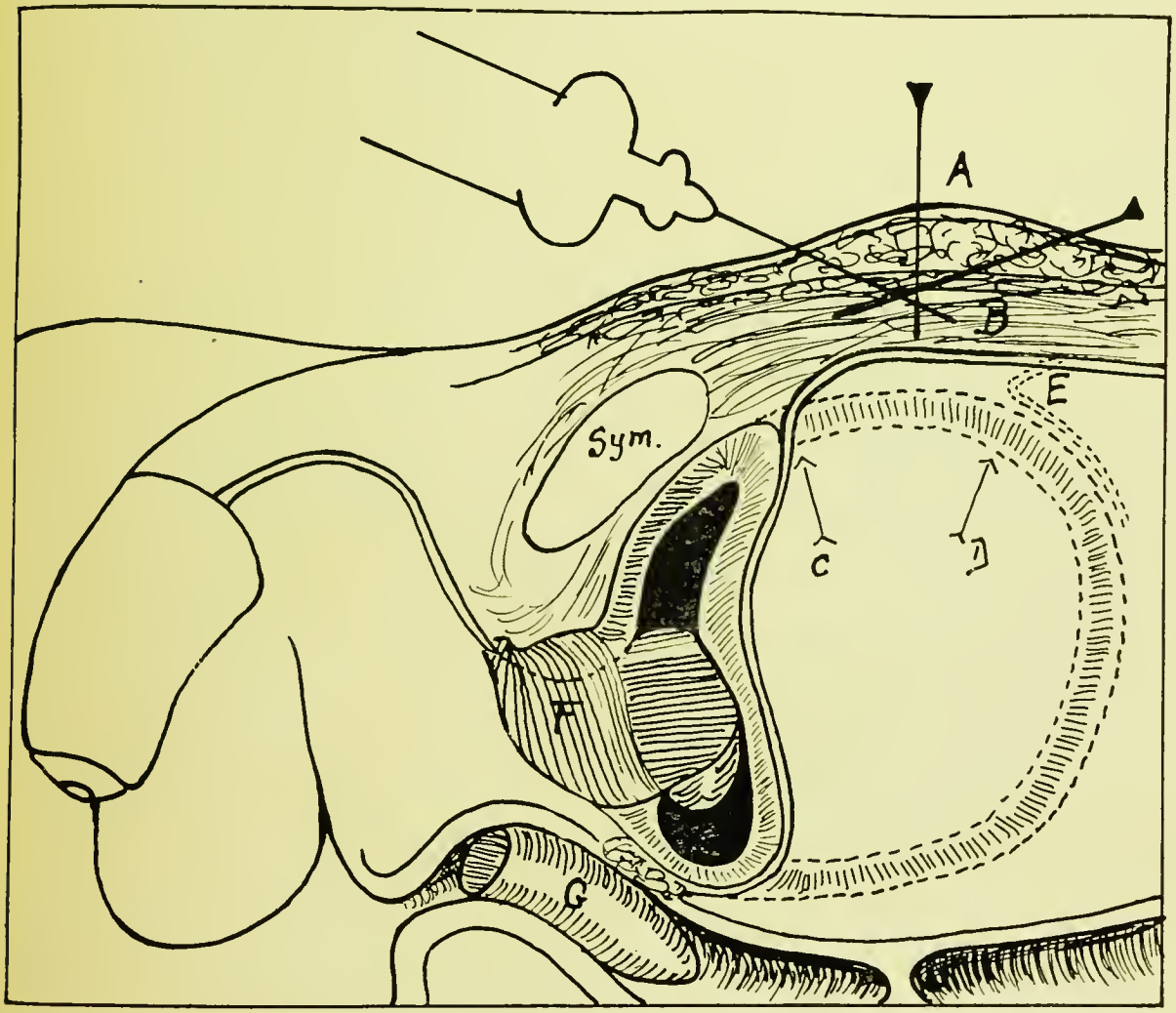


Figure 2. Technic of infiltrating the abdominal wall. (A) Intradermic wheal, through which all layers of the skin to the full extent of the line of incision are obtunded; (B) Method of infiltrating the rectal sheaths; (C-D) Dilatation of the bladder and (E) Reflection of the peritoneum during dilatation; (F) Prostate and sheath; (G) Suppository of anesthesin introduced before operation to obtund the anal reflexes and permits introduction of finger without discomfort.

such cases will soon show sufficient improvement to safely permit the final step in the operation.

TECHNIC FOR SUPRAPUBIC CYSTOTOMY

For the suprapubic cystotomy the bladder cision; it is quicker, takes less solution and produces a more profound anesthesia. To do this quickly and accurately requires some little skill and delicacy of technic, which, however, can be readily acquired with a little practice and careful attention to detail.

Infiltration.—This is done in the following manner: An intradermal wheal is produced in the skin about the middle of the proposed incision, this is used as a station, a long fine needle is entered at this point and directed upward under the skin in the subcutaneous tissues injecting as the needle is advanced the full length of the proposed incision, the needle is partly withdrawn and directed downward in the opposite direction toward the pubes and the tissues here similarly infiltrated. The needle having once entered the skin is not withdrawn completely until the entire field is injected, by partly withdrawing it its point can be directed in different directions, as all parts of the field can be easily reached from a common point of injection, in this way the unnecessary trauma from repeated punctures of the skin is avoided. During the passage of the needle through the tissues the precaution is observed of continuously injecting the solution when the needle is being advanced. This has the advantage of insuring its more uniform distribution as well as avoiding the puncture of any small vessel which may be encountered.

It is preferable to use a 5 or 10 cc. syringe with slip joint connection, with the needle so that the syringe can be readily detached for refilling, the needle remaining in situ.

Having infiltrated the subcutaneous tissues the needle is partly withdrawn and its point directed downward in the mid-line toward the rectal sheath, which is recognized as the first plane of resistance which the needle encounters beneath the subcutaneous tissues, this is gently penetrated at two or three points and the interval between the recti infiltrated. In making these last injections care should be taken to insure their being made in the mid-line; if made decidedly to one side in the case of a well-developed rectal sheath it may be largely retained within the sheath and not diffuse sufficiently to the opposite side, resulting in an unsatisfactory anesthesia.

Having infiltrated the interval between the recti, the needle is advanced slightly further and the posterior sheath gently penetrated; this offers slightly less resistance to the needle than the anterior sheath. With a knowledge of the anatomy of the part and some experience in injecting the different planes of tissue one acquires a certain proficiency and knows with certainty the position of the needle point at all times. For all deep injections it is preferable to use a fine needle with a sharply beveled point, such as is used for spinal puncture, rather than the usaul long tapering point which has many disadvantages for this work.

The degree of distention of the bladder and general adiposity of the individual influence the depth to which the needle should penetrate the posterior sheath at the different levels; should a needle such as is described above enter the peritoneal cavity no harm will result, particularly if the added precaution is taken of always injecting the solution when the needle is being advanced.

In the ordinary case with the bladder moderately distended I usually make three subrectal injections; one three inches above the pubes which just penetrates the posterior rectal sheath, at two inches above the needle penetrates about one-half inch beyond the sheath, a last injection made just above the pubes penetrates about one inch beyond the posterior rectal sheath; about two drams of solution is injected at each of the above points; this completes the deep injections. If any uncertainty is felt regarding these last deep injections they can be omitted until after the recti are separated and the parts brought into plainer view. Ordinarily unless the subcutaneous injection has been very free and sufficient time allowed for its diffusion outward toward the skin it will be necessary to inject the skin which has been purposely left for the last; this is done intradermally along the proposed line of incision, starting at the wheal first produced. The idea in making the deep injections first and the skin last is to allow the deeper injections slightly longer time to diffuse and thoroughly saturate the surrounding tissues.

Operation.—After the incision the parts are gently retracted, progressively advancing until the bladder is reached; the cellular tissue over it is divided and pushed up with the peritoneum out of the danger zone. In making this suprapubic incision it is advisable not to approach too closely to the pubis, but to keep one or two inches away from this point—the distance depending upon the size of the bladder—and yet the incision must not be too close to the peri-

toneum. This method has the advantage of avoiding the possible danger of suppuration in this space and facilitates the more rapid closure later of the fistulous opening, for the nearer these openings are to the peritoneal reflection, the quicker seems to be their closure.

trated before being incised—one stitch on each side fixes the upper part of the bladder to the posterior rectal sheath. The bladder is then freely irrigated and its cavity explored determining the size and shape of the intravesical projection of the prostate, removing calculi

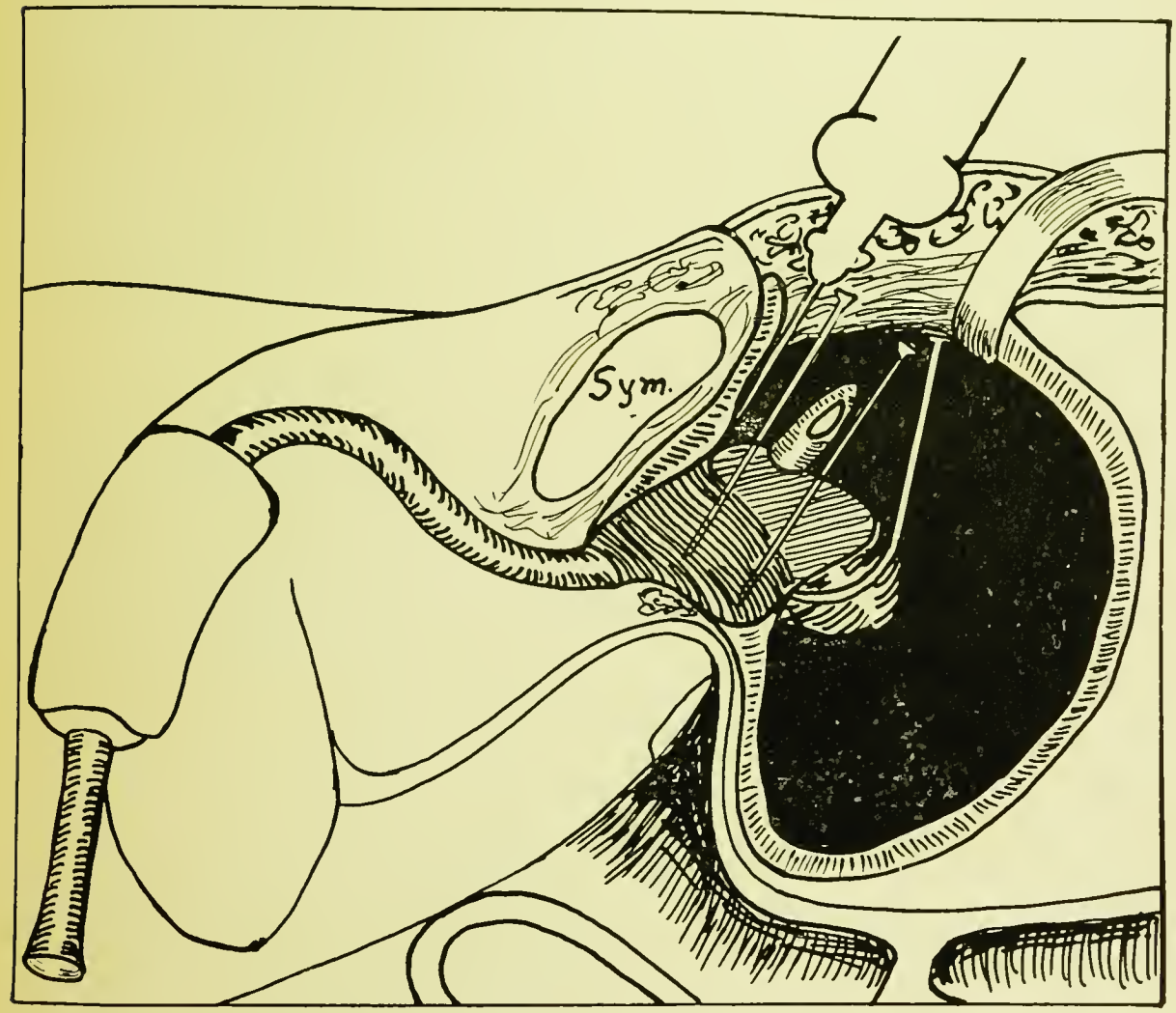


Figure 3. Cystotomy complete and bladder retracted. Injections into the bladder wall above the urethral opening; into the sheath of the prostate on either side and below, (with a curved needle, when necessary), and the finger in the rectum pushing the prostate up into view to facilitate injections of the analgesic solutions. Catheter in position. If the trigone is extremely sensitive, the catheter may be partially withdrawn and injections made into the urethral opening on either side.

Those suprapubic fistulæ which have been difficult to close have always been close to the pubes.

The superior bladder-wall it not, as a rule, very sensitive but it should be lightly infil-

should they exist, and obtaining any other information which may be necessary. If a direct visual inspection is desired in cases in which complications are suspected, this can be easily accomplished by evacuating the contents of

the bladder and by placing the patient in the Trendelenburg position, air will enter and dilate the bladder and its interior can thus be freely inspected by gently retracting the incision. Or, if preferred, a short proctoscope with light attached may be passed within the cavity.

Intravesical Anesthesia.—If much intravesical examination is necessary, or it is desirable to examine the vesical cavity digitally, some form of intravesical anesthesia then becomes necessary. For this purpose I have found it both inadvisable and unnecessary, as well as ineffective, to attempt to anesthetize the interior of the bladder for cystotomy and suprapubic manipulations within it by filling it a short time before with anesthetic solutions. This procedure is now resorted to only for cystoscopy. For all manipulations and operations within it, direct injections are made into, or around, the field to be operated.

The particular sensation with which the bladder is endowed and which is felt upon any abnormal contact with its walls, either internally or externally, is that feeling which we term the desire to urinate. This feeling is more easily excited by manipulation from within and always more acutely toward the vesical neck and prostate region. Pain is only complained of when these manipulations have been rough or when actual trauma has been inflicted. The introduction of a finger within the bladder for purposes of exploration excites a desire to urinate and this desire may become particularly urgent and always becomes so when the parts near the vesical neck are touched. It is not a pain but still may be quite unbearable and demands some effective method to control it. This is accomplished in but a few moments of time. The bladder is first well irrigated and then emptied; with the patient in the Trendelenburg position to dilate the cavity and bring its base into plain view, the anesthetic solution is injected with a long, fine needle at four or five points around the vesical neck, injecting about one-half dram at each point. The needle is advanced just through the mucous membrane with a quick thrust, injecting the solution as the needle is advanced. Unlike the skin and most other tissues the bladder, unless inflamed, is tardy in recording its sensations and anesthesia results before any sensation is felt from the punctures. Ordinarily these injections around the vesical neck are sufficient for all intravesical manipulations, which can now be undertaken with the greatest freedom. However, in complicating conditions where the lateral walls are to be operated upon, further infiltration around the field becomes necessary. But as most nerves reach the bladder near its base and around the vesical neck, the injections made here are most effective in controlling its sensation.

If the case is one that does not come within the class requiring a two-stage operation, but the patient is in fairly good physical condition with good kidneys and with but little residual urine and no bladder infection, the prostate may be anesthetized and removed at once.

PREPARATORY MEDICATION

Whether this be done in a one or two-stage operation, certain preparatory measures are advisable. One hour before operation a suppository containing 10 grs. of anesthesin is placed in the rectum to anesthetize this region and prevent any discomfort when the finger is introduced here in elevating the prostate; at the same time, one hour before operation, a hypodermic of morphin 1-6 gr. and scopolamin 1-150 gr. is administered to lessen physical disturbances.

TECHNIC OF THE SECOND STAGE OPERATION

Infiltration.—If the case is one in which a cystotomy has previously been done, the Pesser catheter or tube is removed from the suprapubic opening. The wound is found presenting a granular surface sloping down toward the vesical opening. This is most effectively and quickly anesthetized by passing a fine needle through this granular surface and injecting just beyond. By beginning these injections above, under the skin margin, the needle can be advanced obliquely in several directions, creating a zone of anesthesia just external to this wall of granulation tissue, which will diffuse in all directions, blocking nerve fibers which come into the field. This is done on both sides and carried down to the vesical opening. Injections are similarly made above

and below the limits of the wound in the subcutaneous tissues in the median line, as the wound has probably contracted and will have to be enlarged. The passage of a fine needle through this granular tissue causes no pain and for that reason is preferred to passing the needle from the skin down. A finger is passed into the bladder to outline its upper limits and determine the proximity of the peritoneal cavity above. Additional injections are now made into the upper wall of the bladder with the finger within guiding the point of the needle.

The bladder opening is enlarged and the patient placed in a moderate Trendelenburg position. After the bladder is well irrigated and emptied, either with a large syringe or sponges, its walls are then retracted by long, deep, narrow retractors, bringing into view the field of the prostate. Depending upon the size and shape of the prostate, several points are selected for injection on the vesical surface, usually one below the opening of the urethra, near the base of the gland, and one on either side. The needle is passed through the mucosa, with the idea of making the injection between the true and false sheath of the prostate, as it is in this plane that the solution must diffuse around the gland, and it is in this plane that its enucleation is effected. It is here where the large venous plexuses are situated and where the nerve-filaments are more easily reached as they pass through to the prostate.

Two or three drams of a 1-2 per cent. novocain solution, containing 10 minims of adrenalin to the ounce, are injected at each of the above points. The needle is then passed into the urethral opening and the lateral wall pierced first on one side and then on the other, and similar injections are made at these points. During these injections the finger is kept within the rectum to better guide the passage of the needle around the prostate where its point can be felt passing between the gland and its false capsule; it also facilitates these injections by elevating or manipulating the gland and guards against the penetration of the false capsule by the needle.

If the gland is very large, or there is much of a projection above the urethal opening, an additional injection can be made here. Otherwise the above will prove sufficient. It is well now to wait two or three minutes for the solution to diffuse and thorough anesthesia to be established before beginning the enucleation. While waiting for the solution to diffuse, the action of the adrenalin is observed in the prostate, which becomes quite pale and bloodless.

Anatomical Difficulties.—Occasionally a case is met with in which anatomical difficulties, such as are encountered in a deep pelvis with sagging and overhanging bladder-walls, make the exposure of the prostate region difficult and requiring much manipulation or deep retraction. Such cases are best handled in the following manner without the loss of time in useless tentative methods; with moderate retraction of the upper portion of the bladder-walls, the long fine needle is entered at the upper edge of the bladder mucosa just back of the pubis and progressively passing downward toward the prostate an anesthetic tract is produced in much the same manner as a tract on the skin is anesthetized, this tract can be made to run over the surface of the prostate or pass just to one side toward the base as preferred.

The same thing can be accomplished by passing the needle down submucously injecting as it advanced until the prostate region is reached. In this way we approach the prostate by an anesthetic pathway and easily reach the sensitive region at the neck of the bladder and the points from which the sensibility of practically the entire bladder can be controlled. The anesthetic area around the vesical neck can be enlarged as required and the deep injections around the prostate made through this anesthetized area. The adoption of the above method will often be found to solve the difficulties in reaching an inaccessible prostate.

In making the deep injections, should they be made into the substance of the gland itself no harm will be done, only they are not quite as effective as when injected peripherally between the true and false sheath; any excess of the solution thrown into the gland in this way is removed during its enucleation and not absorbed. Following these injections a catheter is passed into the bladder. The enucleation of the gland can now be undertaken by any method preferred by the operator and will be absolutely free from all pain or other discomfort. If the intraurethral method is chosen the passage of the catheter can be omitted until

later, but I have always found its presence a convenient guide to the location of the urethra during the different stages of the operation.

Control of Hemorrhage.—A most striking feature is the absence of all bleeding, only a few sponges being slightly soiled, the loss of blood amounting to not more than one or two drams at most. There is no blood to swab out of the bladder afterward.

The cavity left by the prostate is now packed with a Mikulicz pack. This is done in the following manner:

The catheter which has been left in the uretha is now utilized to draw through the uretha, from the bladder outward, a stout piece of silk which has been doubled and passed through a plug or pad of iodoform gauze arranged somewhat cone-shape and about the size of the cavity left by the removed gland. The silk thread is long enough to reach beyond the glans

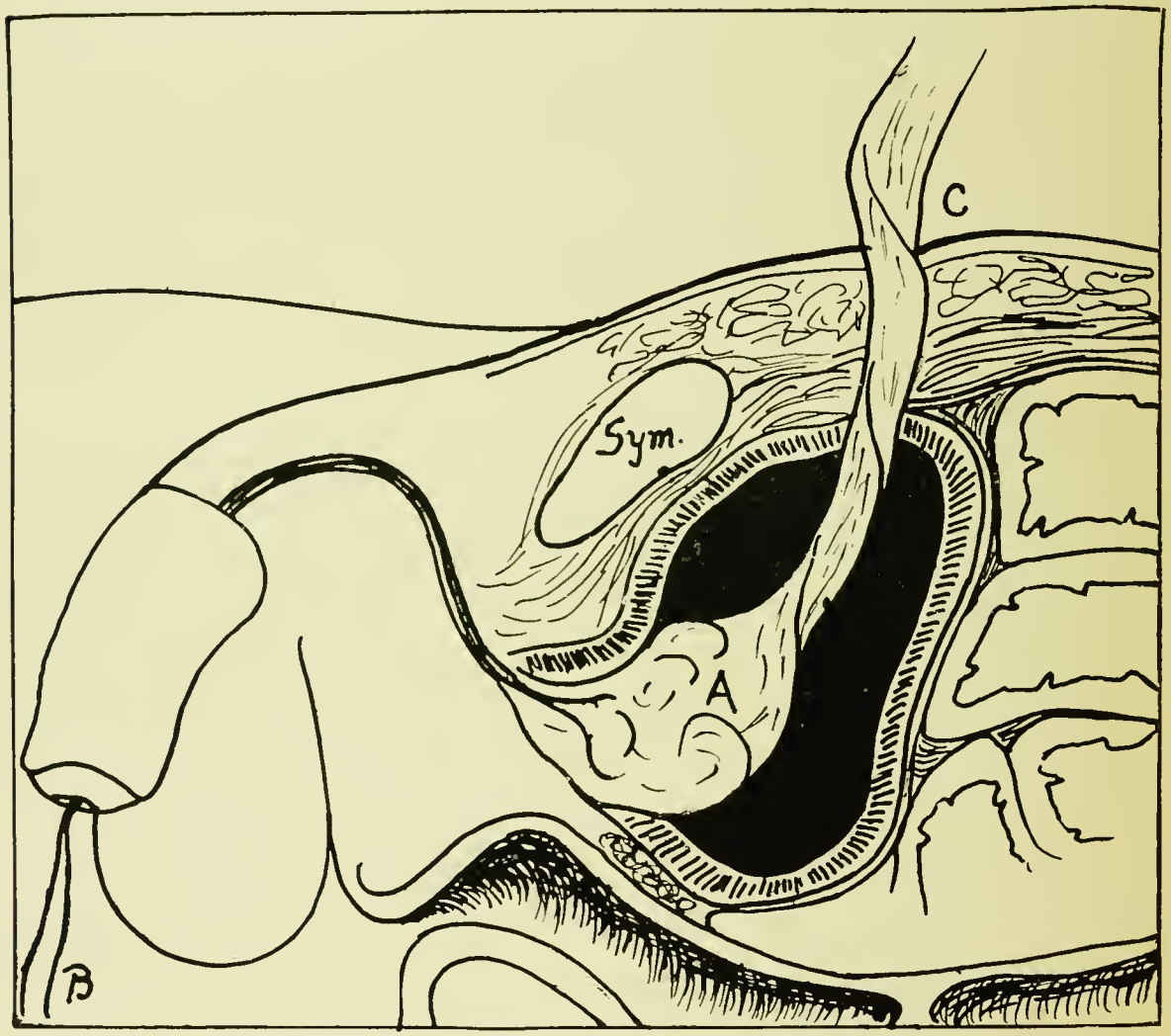


Figure 4. Method of controlling hemorrhage after enucleation of the prostate. (A) Gauze sponge made in folds; (*c*) it is cone shaped and threaded on a silk ligature. This ligature is threaded on the cathether and withdrawn through the urethra, enabling tension to be made on the gauze pack at discretion. An end of the gauze, twisted into a wick is drawn up into the operative wound to facilitate the removal of the pack when desired.

penis and when pulled upon draws this plug effectively into the cavity, thus insuring against any possible secondary hemorrhage. The plug in passing into the cavity also has the effect of turning in any free edge or shreds of mucous membrane against the raw surface of the capsule. One end of the pack is left long enough to protrude through the suprapubic opening to facilitate its removal later. The removal can be simplified by the method of arranging the pack; a piece of gauze is first folded into a strip from one to two inches wide, one end is spread open to make a covering for the remainder which is packed within this outer portion in successive folds, one above the other, the end from the last fold is left long to project from the suprapubic opening. Held in this position each fold is transfixed by the needle and thread. The pack when in position and arranged in this manner is gradually unfolded when the suprapubic end is pulled upon and comes away as a long strip rather than *en masse,* thus making its removal easier and safer.

This is a most effective and simple method of providing against possible secondary hemorrhage, which is impossible when the pack has been properly placed. As the pack is entirely under your control, it can be forced in tighter by drawing upon the urethal string, or loosened by manipulating the suprapubic end. For this valuable procedure I am indebted to my friend and teacher, Professor Matas, who taught me its use and advantages.

A drainage tube placed in the suprapubic opening and a few approximating sutures complete the operation.

The pack is removed in twenty-four or forty-eight hours when danger of hemorrhage is past and the case is handled by the usual methods following these operations.

ADVANTAGES

A notable feature is the absence of all shock or depression, the pulse showing very little change after operation. Often there is not enough pain to justify a hypodermic. These cases are usually up in a chair in a few days and on their feet by the end of a week. The nourishment is usually restricted to liquids for the first day, after which they are permitted to eat what their appetite calls for. Many cases operated by this method show absolutely no after-disturbance of any kind and feel as if they had not been operated at all. The solution used for this work should preferably be novocain 1-2 per cent. in 4 per cent. sodium chlorid solution. Ten or fifteen drops of adrenalin solution 1 to 1000 are added to 3 or 4 ounces of the solution. For the injections around the prostate slightly more adrenalin may be desirable. I usually use about 10 drops to each ounce of the anesthetic solution.

If novocain is difficult to obtain, as is the case at present, the operation can be as satisfactorily performed with eucain or Schleich's No. 1 solution of cocain.

COOPERATION IS THE WATCHWORD OF MODERN PROGRESS. YOU ARE NOT DOING YOUR BIT UNLESS YOU CONTRIBUTE THE ONE THING YOU KNOW BETTER THAN ANY ONE ELSE TO THE SUM TOTAL OF AVAILABLE INFORMATION IN YOUR SPECIALTY. KEEP IN TOUCH WITH THE EDITOR. LET HIM KNOW THE DETAILS OF YOUR LABORATORY EXPERIMENTS AND THE RESULTS OF YOUR CLINICAL EXPERIENCE. HE WILL ACCORD THEM DUE PUBLICITY AND GRATEFUL ACKNOWLEDGMENT.

INJECTION OF THE GASSERIAN GANGLION FOR THE TREATMENT OF TRIGEMINAL NEURALGIA . GENERAL CONSIDERATIONS . ANESTHESIA AND PARALYSIS . REGIONAL ANATOMY OF THE FORAMINA . EXPERIMENTAL INJECTIONS . LANDMARKS FOR INJECTION . INSTRUMENTARIUM . TECHNIC OF INJECTION . SIGNS AND SYMPTOMS FOLLOWING . LIMITATIONS OF THE ANESTHESIA . DANGERS AND TRANSIENT PHENOMENA . HÄRTEL'S TECHNIC . INJECTING THE SUPERIOR MAXILLARY NERVE . COMPLICATIONS AND LIMITATIONS . CONCLUSIONS

BY WILFRED HARRIS, M. D., F R. C. P LONDON, ENGLAND

THE TREATMENT OF chronic paroxysmal trigeminal neuralgia by alcohol injection of the main divisions of the fifth nerve with strong alcohol at their deep foramina of exit at the base of the skull, first brought forward by Schloesser and since described by Ostwald, Lévy and Baudouin, and Sicard, in Paris, by Patrick, in America, and by many others has now become a well-known means of successfully treating this terrible complaint, as a substitute for the somewhat severe operation of gasserectomy or its modifications.

GENERAL CONSIDERATIONS—ANESTHESIA AND PARALYSIS

The difficulty, however, of performing the delicate technic required for the successful injection of these nerve trunks at their deep foramina, and the great patience that may be required in the operation of finding the nerve and injecting it successfully so as to produce dense anesthesia of its area of distribution, have led to many conflicting views as to the efficacy of this treatment and to the effects produced on nerve tissue by the injection of strong alcohol, thus many operators have been content to insert the needle according to instructions given for the average direction of the foramen required, to make the injection at the average depth, or when the needle hits the bone, and then persuade themselves that they have injected the nerve required, even though no anesthesia whatever is produced. Statements have thus been made that neither sensory motor nor paralysis result from injection of a nerve trunk with alcohol, and on this assumption the same treatment of alcohol injection has been proposed and practised for the treatment of sciatica. Fortunately such operators will usually miss the sciatic nerve just as the fifth nerve branches may be missed, and no obvious damage may result, though disaster inevitably follows should the sciatic trunk be injected with strong alcohol, and complete footdrop lasting 12 months or more will reward his efforts. It cannot be too strongly urged upon those who would practice alcohol injection for trigeminal neuralgia that patience and the greatest care in manipulation is necessary, and that until deep anesthesia of the area of distribution of the nerve trunk aimed at has been produced he may be quite certain that his injection has not been placed within the nerve trunk, and that the fault is not with the method, or with the patient, but that the point of his needle has not yet properly reached its objective. The operator must therefore become familiar blindfold with the anatomy of the parts concerned, namely the bones of the face and the bones of the skull. Schloesser's original route to the foramen by injection within the mouth has, I think, been given

up by the majority of workers in this treatment. Personally, I have never used it and consider it awkward as well as unsafe, and I always use the route through the side of the cheek to reach the foramen ovale or the foramen rotundum. The skin can thus be properly sterilized and absolute security from sepsis assured.

REGIONAL ANATOMY OF THE FORAMINA

If a skull with the lower jaw attached be studied, it will be seen that the foramen ovale can be reached with a needle of 2 1-2 to 3 inches in length from two directions through the side of the cheek, firstly through the space beween the lower border of the zygoma and the lower border of the sigmoid notch of the lower jaw, the needle passing almost straight inwards through the zygomatic fossa to reach the foramen ovale in the great wing of the sphenoid bone at a depth of about 1 3-4 inches. In the majority of skulls it will also be seen that if the needle be kept close against the sigmoid notch of the lower jaw that the point of the needle can be made to pass through the lips of the foramen ovale and even to pass through into the cranial cavity. Another route to the foramen ovale will be to pass the needle through the cheek about 1 1-4 inches further forward in order that the needle shall reach the zygomatic fossa in front of the coronoid process of the lower jaw instead of behind it as in the first method described. When using this second route the needle must be passed much more obliquely backwards in order to reach the foramen, and the length of needle required is greater, a 3 1-2 inch needle being advisable. By this route also it will be found that the point of the needle can be made to pass through the foramen ovale into the cranial cavity, indeed more easily than by the posterior route, though I consider the anterior route more difficult on account of the greater depth to which the needle must be sunk, and it is also much more productive of hematoma from the liability of injuring the internal maxillary artery.

EXPERIMENTAL INJECTIONS

After familiarizing oneself with the manipulation of the needle upon a clean skull the next step in acquiring dexterity should be to practice injection of the foramen by each route upon bodies in the post-mortem room. At first it will be advisable to have the calvarium and brain removed, but not to strip the dura mater from the base of the skull. The injection should be then made with as great care in the choice of the direction and insertion of the needle as though a patient were being dealt with, but instead of using ordinary alcohol some colored solution such as methylene blue should be used for the injection in order that the path of the fluid may be perceived after the injection has been made. If the point of the needle has been properly placed within the lips of the foramen ovale it will be found in nearly every case that the colored solution has penetrated along the third division of the 5th nerve into the Gasserian ganglion staining either part or the whole of it deep blue, and if as much as 2 cc. of fluid are injected not only the ganglion may be stained but also the outer wall of the caverenous sinus and the dura mater posterior to these.

As a result of this preparatory work in 1908 I felt certain that it would be possible to inject the Gasserian ganglion in the living patient, with alcohol in many cases, if the needle was correctly placed piercing the 3rd division of the fifth nerve at its exit from the skull at the foramen ovale. Practice on the dead body showed that in the majority of instances when using this route it was possible to work the needle through the foramen ovale either into the ganglion itself or into the cavity of Meckel surrounding the ganglion. If the needle was pushed inwards more than 1 1-2 centimeters through the lips of the foramen the point of the needle would reach the outer wall of the cavernous sinus, and it is therefore of the utmost importance not to attempt to push the needle more than one centimeter beyond the bony foramen. When for the first time I injected the ganglion in the living subject in 1910, I obtained the result in a patient with neuralgia of the 3rd division only, in whom my intention was to inject the 3rd division at the foramen ovale. After making the injection of little over 1 cc. of strong alcohol, somewhat to my surprise I found that the whole area of the 5th nerve in all three divisions on that side was now insensitive to pinprick.

LOCATING THE POINT AND DIRECTION OF INJECTION

My superficial landmarks which I use for reaching the foramen ovale are as follows: With a skin-writing pencil I mark out by palpation the lower border of the zygoma, and also draw a line from the incisura notch above the lobule of the ear to the lower border of the ala nasi. This line roughly corresponds in the majority of skulls with the lower border of the sigmoid notch of the mandible. The space between the lower border of the zygoma and this line marking the sigmoid notch of the mandible delimits the area through which it is possible to thrust a needle into the zygomatic fossa. I next mark out the tubercle on the lower border of the zygoma by measuring 2 1-2 centimeters from the middle of the external auditory meatus. This tubercle can only occasionally be felt distinctly with the finger and I then draw another line through this point vertically to the incisura-ala-nasi line. The plane drawn through this line at right angles to the zygoma and side of the head will pass through the foramen ovale. It would be possible to plunge a needle straight inwards through this line, and reach the foramen ovale at a distance of 4 1-2 to 6 1-2 centimeters, according to the size and squareness of the head, and the thickness of the tissues of the side of the cheek. This is not, however, the best direction to insert the needle because it will be found on looking at the skull that the spine of the sphenoid slopes inwards and forwards to the foramen ovale, the lips of which are directed downwards, forwards and outwards. Consequently a better line for the needle to reach this foramen will be to push it through the side of the cheek somewhat in advance of the plane through the tubercle of the zygoma, about 2-3 of a centimeter in front of the line marking this plane, and the needle is then pushed in a direction very slightly backwards and upwards, so as to reach the plane through the tubercle at the required depth, thus hitting off the foramen ovale. Although this is the average direction for the majority of skulls it will occasionally be found that the direction required to hit the nerve at the foramen ovale may be either rather more acutely backwards and upwards, or on the other hand directly inwards, especially in large square heads.

INSTRUMENTARIUM

The needle which I use is made of steel 7 centimeters long and one millimeter in diameter, with a short point, and a large mount with three rows of milling so that it can be held firmly in the fingers. A brass wire stylet is necessary which should fit the bore of the needle fairly accurately, but does not project beyond its point, the brass wire being bent sharply at a right angle as it emerges from the mount, which is grooved to receive it, in the same line with the bevelled short point. I use two Record syringes of one and two cubic centimeters capacity, the bore of the needle mount being cone-shaped to fit accurately upon the nozzle of the syringes. The larger syringe is filled with 2 cc. sterile novocain solution, and the smaller syringe with 90 per cent. alcohol. The steel needle, which is brightly nickleed when new, I keep in a tube filled with petrol, securely stoppered, as repeated boiling spoils the needles and after some time renders them liable to fracture. After taking the steel needle out of the petrol with sterile forceps it should be syringed through with strong alcohol, and it is then ready for use.

TECHNIC OF INJECTION

After sterilizing the skin by painting with 2 per cent. iodin in spirit solution I then puncture the skin of the side of the cheek with a fine hypodermic needle attached to the novocain syringe, through a point about 2-3 of a centimeter in front of the plane through the tubercle of the zygoma, as previously described above, and on the incisura-ala-nasi line, that is to say sinking the needle through the lowest part of the space between the under surface of the zygoma and the edge of the sigmoid notch of the mandible. Firstly the skin is anesthetized as superficially as possible, and then the hypodermic needle is pushed in gradually injecting a few drops of novocain solution step by step as the needle is pushed in to its hilt. The hypodermic needle is then withdrawn and the syringe put ready for use again when required, and the 7 centimeter steel needle, with its stylet fixed in situ, is now

pushed in through the same puncture in the cheek in the direction of the foramen ovale. The reason for the stylet as I use it is to keep the caliber of the needle from becoming filled with blood clot, inasmuch as if blood gets inside the needle and alcohol is then injected through it a firm hard clot is rapidly formed in the bore of the needle, which may make further injection impossible without taking out the needle and cleaning it.

The needle is pushed in steadily through the cheek and internal pterygoid muscle, the right hand so manipulating the mount of the needle as to keep its general direction very slightly upwards and very slightly backwards, almost straight inwards, passing through the zygomatic fossa so as to hit the under surface of the sphenoid bone at a depth of about 5 centimeters, slightly less or slightly more according to the fatness of the cheek and size of head.

In one patient with a particularly big head I had to pass the needle inwards to a depth of 6 3-4 millimeters before reaching the nerve at the foramen ovale. No force should be used in pushing in the needle, slight steady pressure only being employed, as it is most important that the needle should not be broken. For the same reason the patient should be warned against making any chewing movements with the jaw during the operation. Indeed, to abolish nervousness on the part of patients so that they may keep still and placid during the process of searching for the nerve, I usually give them a preliminary injection of morphia 1-4 gr. with hyoscin 1-150 gr. 20 minutes before I make the first puncture of the cheek. This injection produces drowsiness but not unconsciousness, and the patient is able to answer questions and tests for anesthesia with perfect readiness, but is yet able to bear even prolonged searching for the nerve for 1-2 an hour or more with equanimity.

SIGNS AND SYMPTOMS OF THE INJECTION

If the needle should happen to hit the nerve at the foramen ovale when it is first pushed to the required depth the patient will almost invariably give definite indication of the nerve being struck, showing signs of pain and flinching, and often saying that he feels an electric thrill in the lower lip, jaw, or tongue. By no means, however, does this puncture of the nerve at the foramen ovale always produce the subjective sensation of thrilling along the distribution of the nerve, many patients complaining only of local pain in the region of the needle point. In order to test whether the needle point is really within the nerve I carefully remove the stylet without removing the needle, then fit on the novocain syringe, and slowly inject about 0.5 cc. Even though the puncture may not have produced the characteristic thrilling along the distribution of the nerve to the lip and tongue yet the novocain injection may do so, and after waiting for two minutes I then test the lower lip, tongue and chin with a pin point for anesthesia. In many cases I have seen dense anesthesia of the distribution of the nerve produced by novocain injection, increased to absolute anesthesia by the subsequent alcohol injection, without any indication being given by the patient of any other pain or sensation than local in the region of the needle point. This is an important fact to recognize, as otherwise the operator might be tempted to withdraw his needle without having first tested by novocain injection, and to try again for the nerve in different directions. If when the operator thinks he may have punctured the nerve, and yet novocain injection produces no numbness whatever of the lip, it is then certain that the needle point is not within the nerve, and it is of no use to inject alcohol as yet. The needle should be pushed very slightly deeper, and unless this produces pain deeply in the ear, a few drops of novocain should again be injected, and anesthesia tested for as before. If none is produced then the needle should be withdrawn about half its length, and slightly different directions both more backwards and more forwards should be tried until an indication of the nerve being struck is obtained, then repeating the procedure already described.

In patients with long narrow heads and thin faces the direction may be at an angle of at least 20° backwards, and it is a good plan if the first puncture does not reach the nerve to withdraw the needle partly and change its direction slightly backwards, so as to hit the spine of the sphenoid with the point of the needle at a depth probably of 3 1-2 to 4 centimeters. This spine slopes inwards towards the foramen ovale, and the needle point should be edged along it forwards until it slips off the

bone towards the foramen. The nerve may often be found at once in this way, but in quite a number of cases when the needle has been directed too far backwards the patient will complain suddenly of sharp deep pain within the ear. This is a sign that the eustachian tube has been pricked, and no injection whatever should be made at that point, or eustachian deafness and tinnitus lasting for many months, and perhaps middle ear abscess may be produced. The needle should at once be withdrawn a short distance and its direction altered slightly forwards and the nerve again searched for. Another slight accident liable to happen in this region when the needle is pushed in too deeply is to penetrate the inner wall of the pharynx, the patient complaining of pain in the throat, and any injection made will be instantly felt on the back of the tongue, causing a slight choking. If this occurs the needle should be immediately withdrawn a short distance and the nerve slowly searched for again. No harm results from such puncture of the pharynx except sometimes slight soreness of the throat for a day or two.

Occasionally in spite of repeated trials in different directions, success in finding the nerve has not yet been achieved. It will then often be a good plan to withdraw the needle partly and to change its direction slightly forwards and horizontally, then push it inwards until it strikes bone. This is the external pterygoid plate which is a useful landmark of the required depth of the foramen, which lies behind and very little deeper than the base of this plate of bone where it joins the sphenoid. In order then to reach the nerve the needle must be edged backwards until it is felt to slip off the posterior edge of the external pterygoid plate. The direction of the needle should now be carefully noted, and its point should be raised slowly by lowering the mount, and the needle pushed inwards and backwards to the base of the skull, when the desired result may be achieved.

METHOD OF INJECTING THE ALCOHOL

When injection with novocain solution produces anesthesia of the lower lip and tongue, we then know the needle is correctly placed and keeping the needle as still as possible, the alcohol syringe is substituted for the one with novocain, fitted on to the needle mount and the alcohol is injected slowly drop by drop. This will produce a burning pain in the distribution of the nerve, the patient often saying that the jaw and lip feel as though on fire. This sensation does not last very long, about 30 seconds, fading gradually away and then disappearing entirely, only to be reproduced with the next push of the piston injecting more drops of alcohol. With each few drops of alcohol the burning sensation becomes less intense and when 3-4 to 1 cc. of the alcohol have been injected no further burning may be produced. Enough has now been injected, but the needle must not be withdrawn until the lip, chin and tongue have been tested by pinprick. These should be completely anesthetic so that pressure with a pin upon the lower lip and chin or the half of the tongue on that side should not be perceived at all. When this result has been achieved the needle is at once withdrawn, and firm pressure maintained with a sterilized swab upon the puncture point for a minute or two in order to arrest any slight bleeding there may be and to prevent the formation of hematoma. There is practically no danger of puncture of any important vessel during the process of searching for the nerve with the needle. The only vessel that may cause hematoma in this region is the middle meningeal artery, which enters the skull through the foramen spinosum just posterior to the foramen ovale. This vessel may therefore be punctured by the needle if it is directed too far backwards. The indication of this may be swelling of the side of the cheek which may even be seen to pulsate slightly, and escape of blood through the needle if the stylet fits at all loosely. When this occurs the needle must instantly be withdrawn and firm pressure made with sterilized swabs over the site of the puncture for about five minutes; if this is done no hematoma of any consequence will result and searching for the nerve may then be proceeded with again. Before reinserting the needle, however, its caliber must be carefully cleansed from blood, or the injection of alcohol will subsequently produce a firm hard clot within it. The only dressing necessary is a patch of collodion gauze the size of a dime over the needle puncture, which should be left on for three days.

LIMITATIONS OF THE ANESTHESIA

When the injection has been limited to the third division of the 5th nerve at the foramen ovale, and has not penetrated backwards through the nerve into the Gasserian ganglion, the anesthesia will be strictly in accordance with the anatomical distribution of the nerve. Thus, half the tongue, exactly, as far back as the circumvallate papillae will be completely anesthetic, the gum and lower teeth on that side as far back as the anterior pillar of the fauces will be likewise numb, the lower lip and chin on that side, the strip along the cheek supplied by the buccal branches, and the area of the auricular temporal nerve, a pear-shaped area with its narrow end below at the level of the incisura notch and spreading upward on the temple and side of the scalp. The numb area supplied by the auricular temporal nerve will also include the anterior and upper portion of the pinna and the anterior wall of the external auditory meatus, and also the outer surface of the tympanum, which though not completely anesthetic may now be touched with a probe or other instrument without the patient objecting. The motor branch of the 5th nerve which issues from the foramen ovale beneath the larger sensory 3rd division will also be paralyzed, the temporal, masseter and pterygoids being the only important muscles affected.

SYMPTOMS FOLLOWING SUCCESSFUL INJECTIONS

Owing to their paresis there will be some weakness of chewing on that side and on opening the mouth the lower jaw will fall towards the paralyzed side. Owing to the anesthesia of the tongue and of the inside of the lower cheek and lip, there is a danger for the first few days of the patient biting the tongue or cheek severely without being aware of it, if allowed to eat solid food. After three days or so the patient gets accustomed to the numbness and the risk of this damage disappears. Later some wasting of the temporal and masseter muscles may be noticed, the arch of the zygoma appearing especially prominent.

In the majority of cases this motor weakness will recover earlier than the sensory paralysis and may not be noticeable after two or three months, though in cases properly injected the anesthesia of the lip and tongue may persist for 18 months or even longer. Owing to the anesthesia of the half of the tongue and of the lower jaw, gum and cheek on one side, patients invariably eat on the sound side, and so any weakness of the masseter and temporal on the injected side matter less.

TASTE—In the large majority, about 85 per cent. of the cases of 3rd division injections in which I have produced deep anesthesia, not only is one-half of the tongue anesthetic to touch and pinprick, but I have also found complete loss of taste to all forms upon that side, certainly as far back as the circumvallate papillae, and in many cases taste is impaired somewhat upon the back of the tongue also. This loss of taste is very definite and striking when properly tested for with the tongue kept out and dried with blotting paper or a clean handkerchief before testing. This loss of taste comes on instantly as soon as the anesthesia is produced, and I have seen it still present 2 years after the injection, though in most cases taste begins to reappear gradually within a few weeks or months as the anesthesia wears off. In a small minority of the cases there will be little or no loss of taste, even though dense anesthesia has been produced.

These somewhat conflicting results I think explain the varying testimony of different authors regarding the path of the nerve fibers for taste.

My results leave no possible doubt but that the taste fibers of the tongue in the large majority of cases reach the pons via the 3rd division of the 5th nerve at the foramen ovale, probably reaching the otic ganglion by the small superficial petrosal nerve from the geniculate ganglion on the facial, thus continuing the chorda tympani fibers serving taste sensation. There must, however, be an alternative path in a minority of cases, in whom possibly the taste sensations are continued from the geniculate ganglion to the gustatory nucleus in the medulla via the pars intermedia of Wrisberg.

SYMPTOMS FOLLOWING INJECTION OF THE GASSERIAN GANGLION

As I stated earlier in my article, in quite a number of cases injection of the Gasserian ganglion may be accomplished at the same time as the 3rd division of the nerve is injected at the foramen ovale, without pushing the needle further through the foramen into the ganglion. The first sign that the novocain, or alcohol, as the case may be, has penetrated beyond the 3rd division into the ganglion itself will usually be that the patient complains of pain in the cheek and nose and eye. As more alcohol is injected it will be found on testing with a pin that the upper lip and cheek are now becoming anesthetic, and that a pinprick is either not felt at all upon the forehead, or is only perceived as a touch. The amount of alcohol required for injection of the ganglion, to produce complete 5th nerve anesthesia I have found to vary between 0.75 cc. and 2.5 cc.

With complete anesthesia thus produced the conjunctiva and cornea become totally anesthetic and firm pressure upon the eyeball is totally unperceived by the patient. In addition to the loss of tactile sensation and to pinprick over the anatomical distribution of the nerve there is also complete loss to pressure upon the forehead and scalp, eye, cheek, and lips, and half of the tongue. Inside the mouth both upper and lower jaws are anesthetic, as is also half of the hard palate and the anterior portion of the soft palate, the anesthesia extending backwards to the anterior pillar of the fauces, but not including the tonsil. An interesting point of difference will be noticed during the injection of the ganglion and injection of the 3rd division only. With the latter the anesthesia becomes progressively deeper steadily as more and more alcohol is injected, and when the anesthesia becomes complete it remains so, at any rate for days, and perhaps for weeks and months. During the injection of the ganglion, however, the anesthesia rapidly proceeds to a maximum, with total anesthesia of the whole distribution of the 5th nerve, perhaps after no more than 0.5 or 0.75 cc. has been injected. Then after waiting from 3 to 5 minutes, keeping the needle in situ, it will be found on testing with a pin point that the anesthesia is now beginning to disappear from the forehead and cheek, that is to say over the areas of the 1st and 2nd divisions of the nerve, though the anesthesia will still remain absolute on the 3rd division. A few more drops of alcohol should now again be injected, and again the anesthesia rapidly becomes total, only to fade away again as before on the upper two divisions of the nerve. This phenomenon is no doubt due to temporary paralysis but not destruction of the nerve cells in the ganglion by the alcohol, though presently after this process has been repeated 3 or 4 times and when from 1 1-2 to 2 cc. of alcohol have been injected the anesthesia may remain complete or nearly so.

OCULAR DANGERS AFTER INJECTION

There is considerable risk of keratitis and corneal ulceration, with consequent loss of eyesight occurring if the anesthesia of the cornea remains permanent. Should the anesthesia thus remain permanent half an hour after the injection has been completed so that the patient cannot perceive any pressure upon the eyeball through the upper lid, I always leave instructions that the upper lid shall be fixed down by adhesive strapping from the upper lid to the cheek. So long as the eyelids are kept closed there is no risk of corneal ulceration, particularly if the palpebral sac is washed out daily with warm water and boracic lotion. As soon as sensibility of the eyeball to pressure returns the eyelids may safely be unfastened. If after 3 days no sensation has returned the eyelids may be unfastened during the day, and closed again at night and the result carefully noted. If steaminess of the cornea appears the eyelids should be at once sewn together by horse-hair sutures, after rawing the edges in the middle so that good adhesion shall take place. It may necessary in some cases to keep the lids thus closed for 12 months or more. I prefer strapping for fastening down the eyelids at the commencement rather than the pressure of a pad and bandage or eye shade, as the patient will be apt to open the eyelids underneath the pad, and owing to the anesthesia of the cornea there will be no irritation felt and the cornea may be badly damaged by the rubbing of the pad.

DURATION OF ANESTHESIA

Total anesthesia of the Gasserian ganglion thus produced is comparatively permanent and the relief from the neuralgia will thus be lasting, though after the lapse of months or years some slight return of sensibility may occur. In such cases I have several times noticed that the anesthesia remains deepest and most intense over the 1st division of the nerve and least over the 3rd division. No trophic effects follow the injection, with the possible exception of keratitis.

TRANSIENT PHENOMENA

Among other slight mishaps that may occur from injection of the ganglion is diplopia, which I have seen last for 3 months due to slight weakness of the external rectus muscle. This I accounted for by edema of the ganglion and the outer wall of the cavernous sinus involving slightly the 6th nerve.

In two other cases I have seen sudden faintness produced together with slight facial paresis and nerve deafness on the same side, together with marked nystagmus; in each case this was a transitory phenomenon and had practically passed off within an hour, having completely disappeared by the following day. The explanation of this must, I think, be found in some of the alcohol having found its way along the dura mater over the petrous bone, reaching the facial and auditory nerves, thus causing the facial paresis and nerve deafness, while the involvement of the vestibular portion of the auditory nerve would account for the vertigo and nystagmus.

In another case I have seen anesthesia of the 2nd division of the 5th nerve much deeper than the numbness of the inferior mandibular portion. Possibly this was due to the needle slipping through the 3rd division at the foramen ovale to hit the 2nd division at its origin from the ganglion.

In another case after injection of the 3rd division at the foramen ovale, pushing the needle onwards through the foramen may cause the point to leave the nerve and enter the cave of Meckel. Injection of alcohol now will cause instant severe pain at the base of the skull and back of the head and the needle must be immediately partially withdrawn and an attempt made to work it further backwards in the foramen. Before injecting with alcohol again trial should be made with a few drops of novocain or a few drops of saline.

THE TECHNIC OF HÄRTEL

I have not here referred to a possible danger of pushing the needle too far through the foramen ovale so as to wound the cavernous sinus, but this could scarcely happen if due caution be observed. In order to escape this danger Härtel. in 1912, (Zeit. f. Chirurgie, May 25, 1912), four months after my paper (Lancet, January 27, 1912,) described injection of the ganglion by a more antero-posterior route, passing the needle in front of the coronoid process instead of behind it. A longer needle, not less than 9 cm. in length, will be required, and it should be inserted beneath the prominent angle of the cheek made by the junction of the superior maxilla and malar bone at a point vertically below the anterior border of the ascending orbital process of the malar bone. Sinking the needle upwards at an angle of 30° from the horizontal and 30° inwards the point of the needle should reach the foramen ovale without very much difficulty, taking the external pterygoid plate and the under surface of the sphenoid as guides.

I have used this method when I have been unable to reach the foramen ovale by the route I have already described, but I think it is less easy owing to the extra depth at which it is necessary to work, and there is also a considerable danger with this route of wounding the internal maxillary vessels. These are protected by the ramus of the lower jaw when using the posterior route through the sigmoid notch, as they turn inwards well below the level of this notch in nearly every case.

INJECTING THE SUPERIOR MAXILLARY NERVE

Injection of the 2nd division of the 5th, or superior maxillary nerve, at its point of exit from the skull at the foramen rotundum may be performed by a somewhat similar route. The needle is pushed through the cheek in the angle which can be felt by the finger between the anterior border of the coronoid process and the under surface of the malar bone. This

point is about 1 1-2 cm. posterior to the spot described previously for injection of the Gasserian ganglion by the anterior route. The needle is pushed upwards at an angle of 40° with the horizontal, and backwards in the line of the ascending orbital process of the malar bone, which line should be marked out on the skin as a guide. A 7 cm. needle should be used, and if the needle is made carefully to keep the direction as described it will pass behind the back wall of the antrum of the superior maxilla and in front of the anterior border of the external pterygoid plate, thus passing through the pterygo-maxillary fissure to enter the spheno-maxillary fossa. The foramen rotundum lies at a depth of from 5 to 6 centimeters, and if no indication of the nerve being hit has been shown when the needle has reached this depth, I withdraw the needle slightly and change its direction slightly backwards and feel for the external pterygoid plate as a landmark. Then slipping the point of the needle over the anterior border of the plate it is pushed inwards to a depth of an additional centimeter, taking care to keep the original direction of 40° upwards, when the nerve should be struck.

DANGERS OF THE SUPERIOR MAXILLARY INJECTION

This injection is certainly more dangerous and undoubtedly more difficult than that of the foramen ovale. In addition to the danger of wounding the internal maxillary vessels there is the risk of injuring the 3d or 6th nerves at the sphenoidal fissure, if the needle be directed too high. Another serious risk is injury to the optic nerve, which lies barely more than one centimetre deeper than the foramen rotundum and almost in the same line used for the injection. Central scotoma, diminution of color perception, or a severe degree of blindness in that eye may be produced by varying degrees of damage from injection of alcohol at too great a depth by this route. It is therefore important to feel for the external pterygoid plate as a guide to the depth of the foramen rotundum, and the needle should never be sunk more than 1 1-2 cm. deeper than the anterior edge of this plate when searching for the superior maxillary nerve. Unlike the foramen ovale the foramen rotundum cannot be used for the injection of the Gasserian ganglion.

LIMITATIONS OF THE RESULTING ANESTHESIA

When the foramen rotundum is properly injected there will result immediate and complete anesthesia of the upper jaw and cheek, side of the nose and inside of the nostril and the upper lip, half of the hard palate and of the soft palate nearly as far back as the base of the uvula. In some cases, although the cheek and teeth may be found completely anesthetic, the palate remains sensitive, no doubt owing to the needle having hit the superior maxillary nerve in front instead of behind Meckel's ganglion. In no case of injection of the 2nd division of the 5th nerve, however complete the anesthesia of the cheek and palate, have I ever seen any anesthesia of the temporal branch of this nerve, the anesthesia always ending sharply at the outer canthus of the eye. In addition to the loss to pin-prick and to touch on the cheek, there will be also complete loss to perception of pressure. This effect has already been noted as a result of injection of the Gasserian ganglion, in which pressure will be totally unperceived upon the anterior half of the head and face and eyeball. This fact disproves the theory which has been put forward that the sense of pressure on the face is served by fibers running with the motor facial or 7th nerve, and proves that pressure as well as other forms of sensation on the face and forehead is supplied by the 5th or trigeminal nerve.

SPINAL ANESTHESIA IN THE CAT . SOME RECENT STUDIES IN COMPARATIVE PHYSIOLOGY . INVESTIGATIONS TO DETERMINE THE DIFFUSION OF INJECTED FLUIDS . REGIONAL PARALYSIS . EFFECTS ON BLOOD PRESSURE . REACTIONS . RESULTS OF CERTAIN RESUSCITATIVE MEASURES . CONCLUSIONS FROM THE EXPERIMENTAL DATA

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THE DANGERS AND DISCOMFORTS of ether anesthesia have long been recognized. Inevitable nausea, possible pneumonia, difficult respiration, renal injuries, make ether anesthesia impossible in certain cases, dangerous in others, and distressing in all. To meet these difficulties, spinal anesthesia was devised for use in fields where general anesthesia is superfluous, such as operations on the perineum. As a rule beneficent, spinal anesthesia is nevertheless by exception open to a grave and sudden danger. In the course of surgical procedures otherwise completely successful, the vasomotor apparatus may suddenly give way. The fall in blood pressure is immediate, sometimes profound, always disquieting. Nor can the surgeon predict in what patient it may appear.

The points of interest in this phenomenon are as follows: (1) The extent and the time relations of the fall in blood pressure and the effect of this fall on the efficiency of the central nervous system. (2) The region paralyzed. (3) The structures affected, whether the vasomotor center, the roots of the spinal nerves, the afferent or the efferent paths in the body of the spinal cord. (4) The extent to which the drug may pass along the cord from the point of injection, as modified by the per cent. of the drug in the solution used, the bulk of this solution, the force of gravity, and the possible fixation of the drug by the tissues which it bathes. (5) The duration of the phenomena. (6) The influence of adrenalin. (7) Remedial measures, directed to raising the fallen blood pressure.

Obviously, these factors cannot be studied with complete satisfaction in man, in whom the condition of experimentation cannot be varied at will. We present, therefore, a systematic investigation of spinal anesthesia in animals. The only experimental study of blood pressure in spinal anesthesia so far as we are aware, is that of Gray and Parsons (Quarterly Journal of Medicine, 1911, v, 339), who concluded that the slight fall of blood pressure they obtained in all cases was due to relaxation of the muscles of the abdomen and the lower limbs and that the greater fall obtained in some cases was due to paralysis of the intercostal muscles and the consequent diminution in the pumping power of the chest.

METHOD

Fifty cats were used. In a number of these, two or more intraspinal injections were made, so that, in all, 72 experiments were done. In 18 cases, ether alone was used. In all the animals, the preliminary operations were done under ether anesthesia. In 32 cases, in which muscular reactions would have been a vital source of error, ether was followed by curare. Enough dilute curare solution to paralyze the skeletal muscles was slowly injected through the femoral vein. The carotid blood pressure was recorded by a membrane manometer. Graduation scales for this manometer are shown in Figures 1, 2 and 3. The condition of the vasomotor system and of the sensory afferent tracts was determined by measuring the changes in blood pressure on stimulation of the central end of the brachial and sciatic nerves and on stimulation of the dorsal col-

umns of the cord. The induction currents employed were just perceptible to the tongue. In order to make sure that the drug entered the subdural space, the injection was made under the guidance of the eye. Laminectomy, therefore, was always done at the level of the injection. To determine the spread of the drug by direct stimulation of the cord, laminectomy was often done at other levels as well. A 2 cc. all-glass Luer syringe with 24 gauge needle was used. In the cat, the space between the cord and the dura is so shallow that, except in the lower lumbar region, the needle cannot be inserted perpendicularly to the long axis of the cord without impaling the cord itself. The direction of the needle, whether pointing cephalad or caudad, was found to be a factor of some influence on determining the level to which the drug diffused.

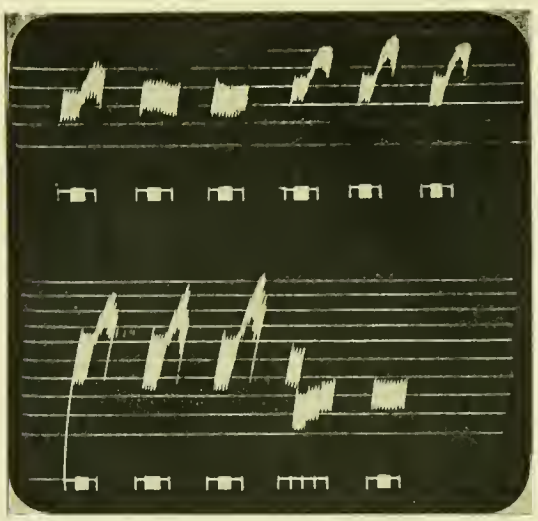

Figure 1. Reduced in size. Injection of 0.01 g. novacain and adrenalin in dilute solution (1 cc.) at Lumbar VII causes paralysis of dorsal columns extending to Dorsal XI, and perhaps above. Brachial rise reduced from 65 to 33 per cent.

Lower curve—left to right

1.	Sciatic stimulation	12.10 p. m.
2.	Brachial stimulation	12.14
3.	Lumabr VII stimulation	12.15
4.	Record of blood pressure	12.17
		(12.22 Injection of drug)
		12.25
		12.28
		12.31
5.	Sciatic stimulation	12.32

Upper curve—left to right

1.	Brachial stimulation	12.35 p. m.
2.	Lumbar VII stimulation	12.37
3.	Dorsal XI stimulation	12.39
4.	Sciatic stimulation	3.25
5.	Lumbar VII stimulation	3.27
6.	Dorsal XI stimulation	3.29

Scale: 50, 70, 90, 110, 130, 150, mm. Hg.

Experiment 45, curarized cat. February 26, 1915.

In most of the experiments undertaken to ascertain the effect of gravity, the foot of the board was raised.

In 35 injections, tablets *C* containing 0.05 g. novocain and 0.000083 g. adrenalin were used; in 18 injections, tablets *D* containing 0.2 g. novocain and 0.006 g. sodium chlorid; in 17 injections, a fluid preparation put up in ampules, each of which contained 1.3 cc. of 5 per cent. tropacocain and 0.00017 g. suprarenin chlorid; and in 2 injections, a fluid preparation in ampoules containing 1 cc. of 5 per cent. tropacocain in 0.6 per cent. sodium chlorid solution. Taking as a test the paralysis of the tissue directly bathed by the drug when injected, the novocain with adrenalin gave 28 per cent. unsatisfactory results, ranging from partial to complete failure; novocain and salt, 38 per cent.; tropacocain and adrenalin, 23 per cent; only two injections were made with tropacocain and salt and both were successful. The percentages of failure were considerably higher than in the clinical use of the same drugs, a difference probably due to the conditions obtaining in experimental work on so small an animal, and to use of inadequate doses in certain experiments.

Following is a typical protocol:

Experiment February 26, 1915. A lightly etherized cat was tracheotomized and cannulas placed in the left carotid artery and the left femoral vein. The left brachial and sciatic nerves were tied and cut distal to the ligature. Laminectomy was done at Lumbar VII and Dorsal XI. The carotid cannula was connected with a membrane manometer.

11.50 a. m. 1.2 cc. 0.5 per cent. curare solution in 15 cc. normal saline solution injected into femoral vein.

This small dose of curare is excreted after artificial respiration has continued some time and the curare must then be renewed.

12.10 p. m. Sciatic nerve stimulated with induction currents. The blood pressure rose from 105 mm. to 170 mm. Hg. (See Figure 1). Stimulation of brachial nerve of dorsal columns at Lumbar VII gave slightly greater increase.

12.17. Blood pressure recorded.

12.22. 1.0 cc. of 1.0 per cent. novocain and adrenalin C (made with distilled water) was injected very

slowly into the dural sac at Lumbar VII. The needle was inserted uerpendicularly to the long axis of the cord.

12.25 Blood pressure has fallen from 100 mm. to 55 mm.

12.28. Blood pressure 65 mm.

12.31. Blood pressure 71 mm.

12.32. Stimulation of sciatic nerve. The reflex change in blood pressure has disappeared.

12.35. Brachial stimulation causes a rise from 75 to 100 mm. (33 per cent.) instead of a rise from 100 mm. to 165 mm. (65 per cent.) shown before novocain.

12.37. No reflex rise on stimulating cord at Lumbar VII.

12.39. No reflex rise on stimulating cord at Dorsal XI.

3.25. Stimulation of sciatic, brachial, Lumbar VII, and Dorsal XI cause normal reflex increase in blood pressure.

In all the experiments, especial care was taken to avoid errors from ether, curare, and artificial respiration. For precautions, see W. T. Porter: The American Journal of Physiology, 1910, xxvii, 281, 282.

CHANGES IN BLOOD PRESSURE

Extent of fall. In Table 1 are recorded 20 experiments in which novocain or tropacocain was injected in the lumbar region in strength sufficient to block all afferent impulses set up by stimulation of the sciatic nerve. In two cases, the blood pressure fell more than 40 per cent. A fall of 40 per cent. is, however, not necessarily alarming. The criterion is not the absolute or percentile fall of blood pressure per se, but whether there remains sufficient blood pressure to carry on, for a time at least, the work of nerve cells in the brain and cord. In one of the two cases just cited, the pressure fell from 150 mm. to 80 mm. Hg., in the other it fell from 100 mm. to 55 mm. The danger line may probably be placed at 60 mm. In only one instance out of twenty, therefore, was there a serious fall in consequence of a lumbar injection.

In the dorsal region, 19 injections were made, in 9 of which the blood pressure fell to 60 or below.

In the cervical region, there were 13 injections and in 5 the blood pressure fell to 60 or below.

In the cat the residual blood pressure, after the extirpation of the spinal cord is from 28 to 31 mm. (Porter and Storey: The American Journal of Physiology, 1907, xviii, 196). In our present experiments, the lowest blood pressure after lumbar injection was 55 (one instance); after dorsal injection, the pressure fell in two cats to 30 mm. and in three cats to 40 mm.; after cervical injection, the pressure fell once to 40 mm. In several instances, therefore, the vasomotor apparatus was absolutely paralyzed and the function lost as completely as if the spinal cord had been extirpated.

TABLE 1

NO.	SITEOF INJECTION	BLOOD PRESSURE	ABSOLUTE FALL	PERCENTILE FALL
	Lumbar	*from to*		
12.....	I	138-105	33	24
20.....	III	100- 90	10	10
25.....	VI	150-100	50	33
26.....	VII	130-100	30	23
28.....	VII	140-130	10	7
29.....	VII	100	0	0
30.....	VII	130-140		
31.....	VII	80- 70	10	12
32.....	VII	120-100	20	8
33.....	VII	170-140	30	18
34.....	VII	130-120	10	8
39.....	VII	90	0	0
40.....	VII	100- 80	20	20
42.....	VII	120- 95	20	17
44.....	VII	160-100	60	38
45.....	VII	100- 55	45	45
47.....	VII	100- 70	30	30
48.....	VII	150- 80	70	47
49.....	VI	120- 90	30	25
50.....	VII	190-170	20	11
	Dorsal			
2.....	XIII	120- 80	40	33
3.....	IX	130- 80	50	38
4.....	II	115- 30	85	74
5.....	IV	120- 75	45	38
6.....	IV	100- 40	60	60
7.....	IV	100- 40	60	60
8.....	IV	120- 75	45	38
9.....	IV	100- 90	30	30
13.....	I	110- 60	59	45
21.....	II	120- 40	80	67
22.....	X	130- 60	70	53
26.....	XII	115- 80	35	30
27.....	XII	80- 50	30	38
29.....	XI	100- 90	10	10
32.....	XII	120- 75	45	38
34.....	X	120- 30	90	75
35.....	IX	110- 80	30	27
37.....	XI	80- 70	10	13
43.....	VI	110- 45	60	55
	Cervical			
14.....	III	125- 70	55	44
15.....	III	100- 80	20	20
16.....	III	90- 60	30	33
17.....	III	95- 40	55	58
18.....	III	80- 60	20	25
19.....	IV —	120- 80	40	33
23.....	III	80- 55	25	31
36.....	III	110-160		
36.....	III	100- 60	40	40
38.....	III	110-100	10	9
38.....	III	120-110	10	8
38.....	III	100- 90	10	10
46.....	II	130- 70	60	46

These instances were, in each case, the result of injection in the dorsal or cervical regions.

Duration of low blood pressure. The injury to nerve cells caused by low blood pressure and the consequent impaired nutrition, depends on two variables; namely, the extent to which the pressure falls and the duration of the low pressure. Recovery from the slight falls in blood pressure usually took place rapidly. After the more severe falls, partial but sufficient recovery took place in from 30 to 90 minutes. *The duration of low blood pressure appeared to depend more upon the amount of drug injected than upon the site of injection.*

Our experiments give evidence that in the majority of instances the vasomotor system was not seriously impaired by the pressures noted in Table I. After 70 to 180 minutes the reflex change in blood pressure on stimulation of the sciatic and brachial nerves returned almost, if not quite, to normal. Thus in Experiment 43, sciatic stimulation caused the blood pressure to rise from 90 to 145 mm., 61 per cent. After injection at Dorsal VI, the pressure fell from 110 to 45 mm. Seventy minutes later, the blood pressure was 70 mm. and on sciatic stimulation it rose to 110 mm., 57 per cent.

THE REGION PARALYZED

It is obvious that drugs like novocain, which are given to interrupt the afferent conducting paths in the spinal cord, may also interrupt the efferent paths. The object in view is to suspend sensations of pain without at the same time suspending some function essential to the well-being of the patient. Such injuries must depend on the importance of the several regions paralyzed. Reflection upon the anatomy of the spinal cord will show that the vasomotor and the respiratory functions are especially to be considered.

The vasomotor function. The reader is reminded that the master cells controlling the tonus of the arteries and thus the weight of the blood pressure are situated in the bulb. Their axis cylinder processes descend the cord in the antero-lateral tracts, bend into the gray matter, and end there in contact with the spinal vasomotor cells. The axis cylinder processes of the spinal vasomotor cells leave the cord in the anterior roots of spinal nerves from the first Dorsal to about the first Sacral. The vascular areas served by these fibers are most of them without importance in the present investigation. Thus in the cat, the sciatic nerve, bearing vasomotor fibers for the hind limb, may be severed without causing any considerable fall in blood pressure. In fact, only the splanchnic nerves, given off from the upper dorsal region, innervate a vascular area large enough to be a dangerous factor in spinal anesthesia. This area, comprising the abdominal viscera, is, however, so extensive as to make splanchnic paralysis very serious, in that the dilatation of the arteries controlled by the splanchnic vasomotor fibers may cause so much blood to enter the corresponding veins that not enough is left in the bulb and cord to support properly respiration and other vital functions. *The rabbit, for example, may be bled to death into its own portal system, by section of the splanchnic nerves.* In studying the regions affected by spinal anesthesia, special attention should, therefore, be paid to that containing the splanchnic fibers. Spinal anesthesia can be successful, only when the afferent paths are paralyzed without at the same time paralyzing enough splanchnic cells or splanchnic root fibers to lower the blood pressure to a degree that may threaten the continued activity of the centers situated in the cervical cord and the bulb.

The importance of the splanchnic area becomes clear when attention is directed to the average percentile fall in blood pressure after injections in the several regions of the cord (Table 1). The averages are: lumbar, 19 per cent.; dorsal, 43 per cent.; and cervical, 27 per cent.

The regional averages just presented, show that the fall in blood pressure, following dorsal injection, is due to paralysis in the splanchnic region and not to paralysis of the bulbar vasomotor center. For, if the fall were due to interference with the bulbar center or with the vasomotor fibers connecting it with the spinal vasomotor cells, the use of novocain in the cervical region, nearer the bulbar center, should cause as great a fall as its use in the dorsal region—at any rate, the fall should not be less.

The conclusion that the vasomotor paralyses of spinal anesthesia are to be sought in the splanchnic area rather than in the bulbar vaso-

TABLE 2

Maximum fall in blood pressure in relation to dosage, region injected, and direction of injection

Fall of 30 Per Cent or Less						Fall of More Than 30 Per Cent					
Experiment No.	Bulk	Per cent.	Level	Needle towards	Per cent. fall	Experiment No.	Bulk	Per cent.	Level	Needle towards	Per cent. fall
	cc.						*cc.*				
17	0.2	4	C. III	Head	5	46	0.2	5	C. II	Head	46
18	0.3	4	C. III	Head	18	16	0.4	2	C. III	Tail	33
						4	0.4	2.5	D. II	Tail	73
9	0.1	1	D. IV	Head	10	8	0.1	1	D. IV	Tail	37
35	0.4	2.5	D. IX	Spine	27	5	0.3	2	D. IV	Tail	37
12	0.5	2	L. I	Tail	24	7	0.1	2	D. IV	Tail	60
11	0.4	2	L. II	Tail	24	6	0.2	2	D. IV	Tail	60
10	0.2	2	L. III	Head	25	43	0.2	5	D. VI	Spine	54
49	0.2	5	L. VI	Spine	25	3	0.5	2	D. IX	Head	38
47	0.5	2	L. VII	Head injected forcibly.	30	2	0.5	1	D. XIII	Head	33
42	0.2	5	L. VII	Spine	16	25	0.2	2.5	L. VI		33
50	0.2	10	L. VII	Spine	10	44	1.0	1.5	L. VII	Spine	37
						45	1.0	1.0	L. VII	Spine	45
						48	0.8	2.5	L. VII	Spine	47

In all the above experiments a mixture of novocain and adrenalin *C.* was used.
Spine means that the needle was pointed at right angles to the long axis of the cord.

SUMMARY

	Injection away from splanchnic area 11 *Experiments*	*Injection in splanchnic area* 14 *Experiments*
Average dose	= 0.0093 g.	= 0.0082 g.
Average bulk	= 0.3 cc.	= 0.42 cc.
Average per cent	= 3.6 per cent	= 2.3 per cent
Average blood pressure fall	= 19.5 per cent	= 45.2 per cent

motor center is further supported by the observations on the fall of blood pressure as affected by the direction in which the injection is made.

Table 2 deals with the fall of blood pressure in relation to dosage, region injected, and the direction of the injection. On the left side of this table are placed the cases in which the fall of blood pressure was 30 per cent. or less; on the right side are those in which the fall was more than 30 per cent. of the initial pressure. In every case in which the fall was30 per cent. or less (except Experiment 35), the injection was so made that the drug was driven away from the area included between Dorsal I and IX (Figures 2 and 3). Contrast Experiment 8 with Experiment 9; in both, 0.1 cc. of 1 per cent. solution of novocain and adrenalin was injected at Dorsal IV In Experiment 8, in which the drug was driven towards the tail, the fall was 37 per cent.; in Experiment 9, in which the solution was driven towards the head, the fall was 10 per cent. Again, in Experiment 16, 0.4 cc. of 2 per cent. solution was injected at Cervical III caudad; the fall was 33 per cent.; in Experiment 4, 0.4 cc. of 2.5 per cent. solution, injected caudad from Dorsal II, much nearer the fall-producing area, was followed by a fall of 73 per cent. The conclusion again appears justified that with moderate but adequate doses, the fall in blood pressure in spinal anesthesia is caused by paralyses in the splanchnic area.

The clinical use of spinal anesthesia is limited to the injection of the drug in the lumbar region. As the drug diffuses towards the head, the first part of the vasomotor mechanism affected by it will be the roots in the thoracic area. It seems justifiable to assume that in clinical, as well as in experimental spinal anesthesia, the fall of blood pressure is caused by paralysis of the splanchnic area.

Paralysis of respiration. Out of a total of 18 experiments in which no curare was used, the injection was made in the cervical or upper thoracic region ten times. In four of these ten injections, the drug was driven towards the tail from a point below the phrenic nerve and there was no paralysis of respiration. In the other six, the drug was injected towards the fifth cervical level; in four of these cases, respiration was paralyzed. In the other two cases, the dosage was very small, (0.1 cc. of 1 per cent., 0.1 of 2 per cent solution of novocain and adrenalin).

In closing this discussion of the regions affected by spinal anesthesia, it is important to answer the very practical question: *How often will surgical anesthesia of the lumbar and sacral region be complicated by a serious fall in blood pressure or by an interruption of the breathing?* In our experiments, there was but one case out of twenty lumbar injections in which the fall in blood pressure (to 55 mm.)

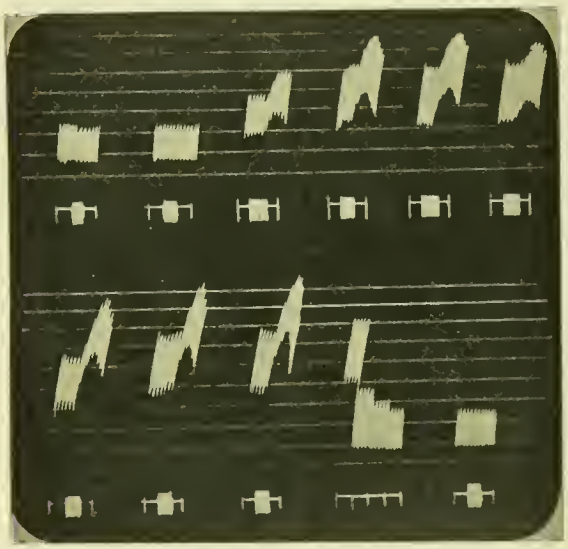

Figure 2. Reduced in size. Injection of 0.01 g. novocain and adrenalin (0.2 cc.) at Dorsal VI causes fall in blood pressure from 110 mm. to 45 mm. in three minutes with abolition of vasomotor reflex from sciatic and brachial.

Lower curve—left to right

1.	Sciatic stimulation	8.55 p. m.
2.	Brachial stimulation	8.58
3.	Dorsal VI stimulation	9.01
4.	Record of blood pressure	
		9.02
		(9.03 Injection of drug)
		9.06
		9.09
		9.12
5.	Sciatic stimulation	9.13

Upper curve—left to right

1.	Brachial stimulation	9.15 p. m.
2.	Dorsal VI stimulation	9.17
3.	Brachial stimulation	9.42
4.	Brachial stimulation	10.12
5.	Sciatic stimulation	10.14
6.	Dorsal VI stimulation	10.15

Scale: 30, 50, 70, 90, 110, 130, 150 mm. Hg.
Experiment 43, curarized cat. February 19, 1915

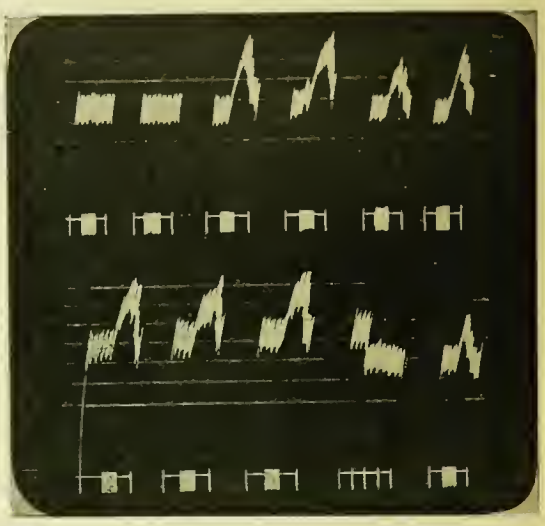

Figure 3. Reduced in size. Injection of 0.01 g. novocain and adrenalin (0.2 cc.) at Lumbar VII causes fall of blood pressure from 120 mm. to 95 mm. in three minutes. Paralysis of sciatic incomplete eleven minutes after injection. Elevation of foot of board at angle of 30°, eighteen minutes after injection, is followed by complete paralysis of sciatic nerve.

Lower curve—left to right

1.	Sciatic stimulation	9.11 p. m.
2.	Brachial stimulation	9.13
3.	Lumbar VII stimulation	9.15
4.	Record of blood pressure	
		9.17
		(9.22 Injection of drug)
		9.25
		9.28
		9.31
5.	Sciatic stimulation	9.33

Upper curve—left to right

1.	Sciatic stimulation	9.48 p. m.
2.	Lumbar VII stimulation	9.49
3.	Lumbar I stimulation	9.51
4.	Brachial stimulation	9.54
5.	Sciatic stimulation	10.22

Scale: 70, 90, 110, 130, 150, 170, 190 mm. Hg.
Experiment 42, curarized cat. February 16, 1915.

might have been serious, and in the eight injections in which no curare was used there was no paralysis of respiration.

Figure 4. Reduced in size. Injection of 0.01 g. novocain and adrenalin (0.2 cc.) at Cervical II cephalad causes fall of blood pressure which is gradual rather than abrupt, due probably to slower action of drug on cord itself than on thoracic roots. Dorsal columns blocked, but vasomotor mechanism below D I is unaffected.

Lower curve—left to right

1.	Sciatic stimulation	9.40 p. m.
2.	Brachial stimulation	9.43
3.	Cervical II stimulation	9.46
4.	Record of blood pressure	
		9.48
		(9.49 Injection of drug)
		9.52
		9.55
		9.58
		10.01
5.	Sciatic stimulation	10.03

Upper curve—left to right

1.	Brachial stimulation	10.05 p. m.
2.	Cervical II stimulation	10.07
3.	Dorsal II lateral surface stimulation	10.12
4.	Sciatic stimulation	11.40
5.	Brachial stimulation	11.43

Experiment 46, curarized cat. March 4, 1915.

THE STRUCTURES AFFECTED

The usual site of paralysis being in the splanchnic area, we should now enquire whether the drug affects the anterior nerve roots or the paths bringing vasoconstrictor impulses from the bulb. We have at present no satisfactory method of isolating effects limited to the splanchnic cells, if indeed the cells are ever paralyzed independently of the nerve paths.

Since paralyses of respiration are so infrequent in spinal anesthesia, we have not attempted to differentiate paralysis of the phrenic root fibers from that of the bulbo-phrenic respiratory path.

It may at once be stated that a strength of the drug sufficient to paralyze the afferent sensory paths (so that stimulation of the central end of the sciatic nerve produces no reflex) will also paralyze the efferent vasomotor fibers (Figure 4). This is illustrated by Experiment 23, in which 0.5 cc. of 2.5 per cent. solution of tropacocain and adrenalin were applied to all surfaces of the cord at Cervical II. The dura at that level was laid open. The blood pressure fell from 80 to 55 mm.; stimulation of the sciatic and brachial nerves and the anterior surfaces of the cord at Cervical III produced no response. Stimulation of the anterior surface of the cord at Dorsal II, however, was followed by an excellent rise in blood pressure, thus proving the integrity of the vasomotor mechanism below the paralyzed portion.

It is possible, on the other hand, to secure paralysis of the nerve roots without disturbing the conductivity of the vasomotor paths in the substance of the cord, as in Experiment 15. In this cat, 0.2 cc. of a 4 per cent. solution of novocain and salt solution *D* was injected at Cervical III. The stimulation of the sciatic caused the blood pressure to rise from 80 mm. to 140 mm., but brachial stimulation caused no rise. The brachial roots in this experiment were paralyzed but the afferent paths conveying sciatic impulses remained unaffected.

There is some evidence to show that different functions may be affected differently. For example, Experiments 2, 3 and 8 showed that the motor paths are paralyzed more easily than the sensory paths.

Experiment 2. 0.5 cc. of 1 per cent. novocain and adrenalin was injected at Dorsal XIII. Stimulation of left sciatic nerve followed by rise in blood pressure throughout experiment, whereas right hind leg was completely paralyzed for 55 minutes.

S. Baglioni (Centralblatt für Physiologie, 1910, xxiii, 869-873), has shown that after the subdural injection of stovain, sensations disappear in this order: pain, cold, heat, pressure; they return in reverse order. This seems to show a varying degree of resistance to the effect of drugs.

Experiments 8 shows that the vasomotor reflex may persist although spontaneous motion of the extremities is lost.

Experiment 8. In an etherized cat, 0.1 cc. of 1 per cent. solution of novocain and adrenalin was injected at Dorsal IV at 12.04 p. m. At 12.31, 12.36 and 12.44, left sciatic stimulation was followed by rise in blood pressure from 105 to 120, 100 to 115, and 110 to 120. The right hind leg remained paralyzed for 65 minutes.

THE DIFFUSION OF THE DRUG ALONG THE CORD

In studying the diffusion of the drug along the spinal cord, it seemed well to fix a reasonable interval between the moment of injection and the testing of the resultant paralysis. This period was set at fifteen minutes, in which time the drug seemed to have exerted its maximal effect. Care was taken not to manipulate the spine after the injection, lest the fluid injected should be pumped or driven to a more distant level. Some writers in this field emphasize movements of the spinal fluid due to the effects of respiration upon the emptying and filling of the cerebro-spinal venous system. That this possible factor in the diffusion of the drug is done away with when the dorsal sac is opened to atmospheric pressure, an operation found essential in our experiments, we are not prepared to deny. Other, and more important, factors affecting distribution within the dural sac can be studied by our method and indeed the problem is simplified by the removal of confusing influences.

Per cent. of drug. In the following experiments, the same quantity of solution was injected, but the solution contained different amounts of anesthetic (a constant mixture of novocain and adrenalin *C*). Paralysis of the dorsal column to direct stimulation was the test employed to fix the limits to which the drug had spread.

Experiment 25. 0.225 cc. of 2.5 per cent. (0.0056 g.) at Lumbar VII diffused 6 vertabrae.

Experiment 42. 0.2 cc. of 5 per cent. (0.01 g.) at Lumbar VII did not diffuse 5 vertebrae.

Experiment 49. 0.2 cc. of 5 per cent. (0.01 g.) at Lumbar VI did not diffuse 2 vertebrae.

Experiment 50. 0.2 cc. of 10 per cent. (0.02 g.) at Lumbar VII did not diffuse 4 vertabrae.

The average diffusion here was less than four vertebrae.

Varying bulk of fluid. In the following experiments the amount of fluid injected was varied, while the percentage of the drug (novocain and adrenalin *C*), remained the same. The paralysis of the dorsal columns was again the test of diffusion.

Experiment 25. 0.225 cc. of 2.5 per cent. (0.0056 g.) at Lumbar VII diffused 6 vertebrae.

Experiment 24, 0.25 cc. of 2.5 per cent. (0.0062 g.) at Lumbar VI diffused 6 vertebrae.

Experiment 4. 0.4 cc. of 2.5 per cent. (0.01 g.) at Dorsal II diffused 9 vertebrae.

Experiment 35. 0.4 cc. of 2.5 per cent. (0.01 g.) at Dorsal IX diffused 11 vertebrae.

Experiment 48. 0.8 cc. of 2.5 per cent. (0.02 g.) at Lumbar VII diffused 8 vertebrae.

The average diffusion was eight vertebrae.

Additional information is afforded by certain experiments in which the drug was injected at approximately the same levels (Lumbar VI or VII), but in which dilute and concentrated solutions are examined with regard to their effect upon blood pressure. The greater the fall, the further the drug progressed toward the splanchnic area.

Dilute Solutions

Experiment 48. 0.8 cc. of 2.5 per cent. (0.02 g.) caused blood pressure to fall 46 per cent.

Experiment 44. 1.0 cc. of 1.5 per cent. (0.015 g.) caused blood pressure to fall 37 per cent.

Experiment 45. 1.0 cc. of 1.0 per cent. (0.01 g.) caused blood pressure to fall 45 per cent.

Experiment 47. 0.5 cc. of 2.0 per cent. (0.01 g.) caused blood pressure to fall 39.5 per cent.

The average fall was 41.9 per cent. The average dose was 0.014 g.

Concentrated Solutions

Experiment 50. 0.2 cc. of 10 per cent. caused blood pressure to fall 11 per cent.

Experiment 41. 0.3 cc. of 5 per cent. caused blood pressure to fall 16 per cent.

Experiment 49. 0.2 cc. of 5 per cent. caused blood pressure to fall 25 per cent.

Experiment 42. 0.2 cc. of 5 per cent. caused blood pressure to fall 17 per cent.

Experiment 40. 0.2 cc. of 5 per cent. caused blood pressure to fall 20 per cent.

The average fall was 17.8 per cent. The average dose was 0.013 g.

The analysis of the observations on diffusion does not show any very definite laws, probably because the number of experiments is necessarily limited. On the whole, the bulk seemed a factor of greater importance than the strength of the solution. Dilute solutions seemed to spread further than concentrated solutions. But in some cases, a dose of small bulk and containing a small amount of the drug produced a more widespread effect than a dose larger both in bulk and in percentage of drug injected in a manner as nearly similar as possible.

Effect of gravity. We are aware of the possibility of error in attempting to determine the effect of gravity upon the diffusion of a drug injected into a dural sac which is exposed at the highest point to atmospheric pressure, whereas normally the cord is protected by its bony envelope. To avoid this source of confusion as far as possible, we tilted the animal and allowed the blood pressure and spinal fluid to become settled after the change of position, before injecting the drug. After the injection, the board was left tilted for fifteen minutes, then returned to level and the dorsal columns were stimulated to determine the extent of the diffusion.

The following experiments compare three animals in the horizontal position with four in which the head was tilted down at a varying angle.

Horizontal

Experiment 42. 0.2 cc. 5 per cent. novocain and adrenalin C at Lumbar VII, did not diffuse 5 vertebrae.

Experiment 49. 0.2 cc. 5 per cent. novocain and adrenalin C at Lumbar VI did not diffuse 2 vertebrae.

Experiment 29. 0.2 cc. 5 per cent. novocain D at Lumbar VII, diffused 3 vertebrae.

Tilted, head down

Experiment 31. 0.2 cc. 5 per cent. novocain D at Lumbar VII, diffused 6 vertebrae.

Experiment 32. 0.2 cc. 5 per cent. tropacocain and adrenalin at Lumbar VII, diffused 7 vertebrae.

Experiment 39. 0.2 cc. 5 per cent. novocain D in 5 per cent. glucose at Lumbar VII, diffused 8 vertebrae.

Experiment 40. 0.2 cc. 5 per cent. novocain C in 5 per cent. glucose at Lumbar VII, diffused 8 vertebrae.

It appears that tilting the animal board at an angle of 40, head down, increases the diffusion of novocain and salt solution, and that the diffusion is increased to a slight degree when the drug is carried in a 5 per cent. glucose solution.

Fixation of the drug. The complete fixation of the drug in some loose chemical combination with the tissues of the cord would be greatly to the advantage of the surgeon. If such a bond existed, the action of the anesthetic would soon be localized. If the paralysis had extended far enough to affect seriously the blood pressure, the patient could then be tilted head down, thus keeping by the force of gravity a supply of blood in the brain. If, however, it can be demonstrated that the drug is not entirely fixed, it would follow that tilting the patient might cause the unfixed remainder of the anesthetic to flow towards the head, invading more of the splanchnic region, and even reaching the phrenic cells, and finally the spinal bulb.

We present three observations upon fixation:

Experiment 34. One cc. of 1.0 per cent. tropacocain and salt solution was injected at Lumbar VII. Twenty minutes later, stimulation of Lumbar I produced a fair rise in blood pressure. Five minutes after that, the dura at Lumbar III was opened. Evidently the manipulation drove the drug upwards, for after that Lumbar I no longer reacted.

Experiment 38. 0.4 cc. of 5.0 per cent. novocain and salt solution D was injected at Cervical III. Blood pressure fell from 100 to 90 mm., but returned to 100 mm. in 13 minutes. Sixteen minutes after the injection, the dura was opened at Dorsal X and as the spinal fluid flowed down the cord the blood pressure fell from 100 to 80.

Experiment 40. 0.2 cc. of 5.0 per cent. novocain, and adrenalin C was injected at Lumbar VII. Paralysis of the sciatic did not occur. Eighteen minutes after the injection, the board was tilted and immediately afterwards complete paralysis of the sciatic was found to have taken place.

From these three experiments we may conclude that after 25, 16, and 18 minutes respectively, enough drug free from fixation was present to paralyze other nerve fibers.

THE DURATION OF THE PHENOMENA

The duration of paralysis of the vasomotor reflexes was studied in relation to the absolute amount of drug injected, and also in relation to the percentage of the drug in solution. In many cases, a low dosage of one of weak percentage (1 to 2 per cent.) secured as long a paralysis as did stronger or larger doses. The minimum dose could not be determined with

any finality, for in one experiment 0.1 cc. of 1 per cent. solution would be fairly effective, while in another a much larger dose would not give the desired effect.

In Experiments 26, 27, 29, and 30, the spinal fluid was drained off 15 minutes after the injection of the solution, but this did not shorten the duration of the paralysis.

In Experiments 5, 6, 8, 20, 21, 22, 24, and as the effects of the drug began to wear off, the stimulation of the sciatic nerve was followed by a fall of blood pressure instead of a rise. In cases in which this phenomenon occurred, the normal reflex returned before the blood pressure rose to its original level.

THE INFLUENCE OF ADRENALIN

In order to learn whether adrenalin was a factor in the phenomena following spinal anesthesia, we twice injected adrenalin chlorid alone.

Experiment 37. 0.5 cc. of 1-10,000 adrenalin chlorid was injected cephalad from Dorsal XI. No change in blood pressure followed, but sciatic reflex was temporarily diminished, perhaps because the solution was cool.

Experiment 38. 0.5 cc. 1-10,000 adrenalin chlorid warmed, was injected caudad from Cervical III. The blood pressure fell from 120 to 110 in five minutes. The reflexes were not affected.

A comparison of the action of novocain and adrenalin *C* with that of novocain and salt solution *D* is given in Table 3. The injection was caudad in Experiment 15 and cephalad in all the others.

Table 3, showing six pairs of experiments, exhibits a markedly greater fall of blood pressure in the cases in which adrenalin was used. This occurs in five of the six pairs. In the remaining pair, the fall of blood pressure with novocain and salt is not great (20 per cent). We do not attempt to explain this fact. It may be that the pressure of salt in solution D is a factor.

It is also noteworthy that although in three experiments the novocain D was more effective as regards duration of paralysis of the reflexes, the average duration of the paralysis after use of D was 40 minutes, whereas, of the four experiments in which C produced paralysis at all, the average duration was 64 minutes. The longest action of D was secured when the solution was made up in 5 per cent. glucose. C failed twice to produce paralysis; D never failed. On the whole, the honors seem to be divided fairly evenly.

MEASURES TO RAISE THE FALLEN BLOOD PRESSURE

In five experiments an effort was made to raise the lowered blood pressure by the intravenous injection of salt solution, adrenalin chlorid or pituitrin. This was done both when the blood pressure was lowered by section of the cord, and by spinal anesthesia. To be of value, such experiments should be done only after section of the cord as otherwise the nat-

TABLE 3

Comparison of action of novocain and salt D and novocain and adrenalin C.

EXPERIMENT	DOSE	LEVEL	TIME OF ONSET ON BLOOD PRESSURE	PER CENT. OF BLOOD PRESSURE FALL	DURATION OF PARALYSIS		PARALYSIS DORSAL COLUMNS	PARALYSIS OF ROOTS
					of blood pressure	of reflexes		
				per cent				
15-D	0.2 cc. of 4% (caudad)	C. III	3	20	25	26	No	Yes
17-C	0.2 cc. of 4% (cephalad)	C. III	3	5	5	0	No	No
29-D	0.2 cc. of 5%	L. VII	0	0	0	25		Yes
42-C	0.2 cc. of 5%	L. VII	3	16	60+	60+	Yes	Yes
30-D	0.2 cc. of 5%	L VII	Rise		0	27	Yes	Yes
49-C	0.2 cc. of 5%	L. VI	9	25	23	28+	Yes	Yes
36-D	0.2 cc. of 5%	C. III	Rise			35	Yes	?
46-C	0.2 cc. of 5%	C. II	12	46	110+	110	Yes	?
38-D	0.4 cc. of 2.5%	C. III	0.5	9	4	20	No	Yes
16-C	0.4 cc. of 2%	C. III	3	33	16+	0	No	Yes
39-D	0.2 cc. of 5% glucose	L. VII	0	0	0	105+	Yes	Yes
40-C	0.2 cc. of 5% glucose	L. VII	3	20	60	60	Yes	Yes

ural return of blood pressure as the spinal drug wears off will influence the results.

Saline solution, in the two experiments in which it was injected intravenously, did not materially affect the blood pressure.

The effect of pituitrin and adrenalin were tried with the cord cut across at Cervical III. Blood pressure stood at 50 in Experiment 36, at 55 in Experiment 38. In Experiment 36, 0.5 cc. pituitrin in 5 cc. H_2O was given. The blood pressure rose in one minute from 50 to 100, and four minutes later had fallen again to 60.

In Experiment 38, 0.5 cc., 1-10,000 adrenalin chlorid in 5 cc. NaCl was given. The blood pressure rose from 55 to 160 at once, but in four minutes after the injection was back at 50.

CONCLUSIONS

(1) In our experiments on spinal anesthesia, there was in twenty animals but one case in which a moderate but adequate injection in the lumbar region caused a fall in blood pressure that might have been serious (to 55 mm.); and in the eight cases in which no curare was used there was no paralysis of respiration after lumbar injection.

(2) Even after marked falls in blood pressure partial but sufficient recovery took place in from 30 to 90 minutes. The duration of low blood pressure appeared to depend more upon the amount of drug injected than upon the site of injection.

(3) The fall in blood-pressue seen after lumbar and dorsal injection is due to paralysis in the splanchnic region. In our numerous observations, it was not due to paralysis of the bulbar vasomotor center.

(4) A strength of the drug sufficient to paralyze the afferent sensory paths in the cord (so that stimulation of the central end of the sciatic nerve produces no reflex) will also paralyze the efferent vasomotor fibers.

(5) The nerve roots may in some cases be paralyzed without disturbing the conductivity of the vasomotor paths in the substance of the cord.

(6) There is some evidence that different functions may be affected differently; thus in three experiments the motor paths were paralyzed more easily than the sensory paths.

(7) Regarding the diffusion of the drug, the bulk seemed on the whole a factor of greater importance than the strength of the solution. Dilute solutions usually but not always spread further than concentrated solutions.

(8) Gravity is a factor of some importance; tilting the animal at an angle of 40°, head downward, increased the diffusion of the drug.

(9) Fixation of the drug is only partial. In three experiments, after 25, 16 and 18 minutes respectively, enough remained free to paralyze other nerve fibers.

(10) In seven experiments, as the effect of the drug began to wear off, the stimulation of the sciatic nerve caused a fall of blood pressure instead of the usual rise. In these cases, the normal reflex rise returned before the blood pressure attained its original level.

(11) A greater fall of blood pressure occurred in the cases in which adrenalin was used in connection with tropacocain or novocain.

(12) Measures taken to raise the fallen blood pressure were of little value. It was easy to restore the blood pressure to normal but the normal level could be maintained but a few minutes.

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GENITO-URINARY OPERATIONS UNDER SPINAL ANESTHESIA . THE COMPARATIVE UTILITY AND SUCCESS OF SPINAL ANESTHESIA . UNTOWARD EFFECTS ON BLOOD PRESSURE . FACTORS AFFECTING THE DIFFUSION OF INJECTED SOLUTIONS . CLINICAL EXPERIENCES AT THE MASSACHUSETTS GENERAL HOSPITAL . DOSAGE . TYPES OF PATIENTS . RESULTS . COMPLICATIONS AND PROPHYLACTIC MEASURES . ADAPTABILITY FOR INTRAVESICAL PROCEDURES . CONCLUSIONS

BY GEORGE GILBERT SMITH, M. D., F. A. C. S. *BOSTON, MASS.*

IT IS A FACT of some historical interest that the first use of spinal anesthesia was for urological purposes. In 1885, Corning,[1] of New York, having first tried it upon a dog, injected 30 minims of 3 per cent. cocain hydrochlorid *"between the spinous processes of the eleventh and twelfth dorsal vertebrae"* of a man addicted to masturbation and suffering from seminal incontinence. Anesthesia of the legs and genitalia was produced. A sound was passed without pain and a urethal electrode applied without inconvenience, although previously the patient had always felt much pain during the passage of instruments. At the conclusion of his report, Corning remarks that he does not know whether or not spinal anesthesia may ever become a substitute for etherization in genito-urinary surgery.

GENITO-URINARY OPERATIONS UNDER SPINAL ANESTHESIA

A review of the literature of spinal anesthesia shows that in a number of clinics this suggestion of Corning's comes very near fulfillment. Dax[2] reports 1,500 cases, of which 168 were genito-urinary, Dunlap[3] reports 1,239, with 585, and Richards,[4] of Cairo, Egypt, reports 500, with 219 upon the urogenital tract. Albarran,[5] in 1908, and Jeanbrau,[6] in 1911, wrote upon the use of spinal anesthesia in urology. The amount of operating done upon the genito-urinary organs in different clinics necessarily modifies the figures, but the literature affords much evidence that wherever spinal anesthesia is used, it is to a considerable extent employed in urological cases.

COMPARATIVE UTILITY AND SUCCESS OF SPINAL ANESTHESIA

A complete discussion of spinal anesthesia is not within the scope of this paper. Only those phases which bear upon its use in urology will be taken up. We must first, however, establish our right to use this form of anesthesia at all. Bevan[7] has recently said that *"spinal anesthesia has little or no field of usefulness. It is dangerous, often incomplete. . . . It should be limited to an exceedingly small field."* With this opinion very few surgeons who have given the method a trial would agree.

Briefly, the position of lumbar anesthesia in surgery seems to be this: the method, if carried out properly on suitable cases, has a mortality no greater than 1 in 1,000. A number of men report considerably more than 1,000 cases without a death attributable to the anesthetic. The statistics offered by various compilers vary from one death in 200 to 1 in 1,800.[8] In many of the cases reported as fatalities, death is clearly due as much to the wretched condition of the patient as to the effects of the anesthetic. With any other method of anesthesia the result would have been the same. There have been reported, however,

enough fatalities undoubtedly due to the anesthetic to make the use of spinal anesthesia unjustifiable in cases in which local anesthesia will suffice, or in which there exist no contraindications to a general anesthetic. The contraindications include not only organic lesions of vital organs, but external circumstances, such as the absence of a reliable anesthetist, or, on the patient's part, an extreme dread of general anesthesia.

The intraspinal injection, it is true, is not always successful. In a few cases with arthritis of the lumbar spine, the needle fails to reach the canal. In other cases, the point may fail to pierce the dura, or having done so incompletely, it may slip out during the injection. These failures are almost always failures in technic, and become less frequent with greater experience. The experience of surgeons generally seems to be that in from 5 to 10 per cent. of the cases in which spinal anesthesia is attempted, the puncture cannot be made successfully or satisfactory anesthesia cannot be obtained.

UNTOWARD EFFECTS

The untoward effects of spinal anesthesia used in properly selected cases are really few. Aside from the matter of ocular palsies, the nervous system is not injured. Eden, Rehn and Spielmeyer (quoted by Rehn[9]) agree that although the drugs used are capable of producing degenerative changes in the spinal cords of dogs into which they are injected in large doses, in man, used in the usual doses, they have no permanently injurious effect. That the amount of drug which we use has no destructive action is proved by Babcock,[10] who has used spinal anesthesia in the same person eleven times within a few years with no ill effects. Another case has been reported into whose subarachnoid space stovain was injected seven times in three weeks, through the mistaken zeal of a house-officer who used it every time he replaced a drainage tube. Riche[11] found that fluid withdrawn from six to twenty-four hours after injection showed no chemical or cytological change. As for the ocular palsies, Reber,[12] in 1910, collected 36 cases from the literature. Twenty-six of these had been followed, and of them 16 had completely recovered, while 5 seemed permanent.

Headache is not an uncommon after-effect, some writers finding it in 20 per cent. of cases. It usually lasts only a day or two, and if persistent may be cured, according to Tuffier,[6] by a lumbar puncture and the withdrawal of 10 to 15 c.cm. of fluid.

As regards the other organs of the body, the toxic effect of the drugs used in spinal anesthesia is negligible. Although these drugs are eliminated by the kidneys, the disturbance of the latter which has been noted[13] is always transient and seldom severe. Miller,[14] studying 16 cases by the aid of phenolsulphonephthalein, found less disturbance than after ether. Albarran, Bier,[15] and Cabot[16] agree that the influence of spinal anesthesia on kidneys, whether healthy or diseased, can be disregarded.

Upon processes in the lung spinal anesthesia has, of course, no effect. That it does not prevent pneumonia has been demonstrated frequently. Von Mickulicz has shown that pulmonary complications occur more frequently after 100 gastric operations done under local anesthesia than after 100 done under ether. We must realize, therefore, that most of the postoperative pneumonias are due to some cause other than the anesthetic. Circulatory congestion, lowered resistance, and septic emboli are the important factors, and they are influenced more by the condition of the patient and the nature of the operation than by the type of anesthesia. In spinal anesthesia the direct effect of the drug upon the heart muscle is insignificant. The effect of vasomotor disturbances upon the heart, on the contrary, is of the greatest importance.

FACTORS AFFECTING DIFFUSION OF INJECTIONS

When a drug is injected into the subarachnoid space, the extent of its diffusion depends upon five factors. The first two are beyond our control. They are (1) the natural diffusibility of fluids, and (2) the circulation of the spinal fluid from natural causes, such as respiration. The other three are more or less within our control. They are (3) the specific gravity of the injection solution, (4) the amount of its dilution with spinal fluid in the

syringe, (5) the force with which the injection is made. A collary to (3) is the position in which the patient is placed after receiving the injection. For a discussion of the question of specific gravity, see Barker,[17] and the more recent experiments of G. G. Smith and V. T. Porter, which follow. As the solution containing the drug diffuses upwards, it paralyzes the nerve-roots which traverse the subarachnoid space. When it reaches the 4th and 5th dorsal segments, the intercostal muscles, according to Gray and Parsons,[18] become paralyzed, and breathing becomes of the diaphragmatic type. If the paralysis extends to the phrenics and the external respiratory nerves of Bell, respiration fails. This catastrophe, however, occurs only rarely, and can be avoided by taking precautions against the upward diffusion of the drug. A good deal has been said about the toxic effect of the drug upon the medulla, and the respiratory and vasomotor centres situated there. Those observers who have studied the question carefully are not strongly in favor of this theory as to the cause of the changes in respiration and circulation, but a satisfactory explanation of the vasomotor phenomena in spinal anesthesia has not yet been advanced. Certainly in some cases the blood-pressure does fall, at times tremendously. We have records of a drop of 100 mm. Hg. Gray and Parsons found a constant fall, with which most other observers agree. This fall they consider to be due to two causes, (1) the flaccidity of the muscles of the abdomen and lower limbs, which are paralyzed by the spinal injection, (2) the change in respiration from costal to the diaphragmatic type. With this change, the diaphragm, they believe presses less strongly on the abdominal viscera, and the suction power of the throax is diminished. Neither this explanation nor the theory of direct toxic effect upon the vasomotor centre seems satisfactory. The fact remains that in a considerable number of cases, the blood-pressure shows a marked fall. This is, to the writer's mind, the most important phase of spinal anesthesia; as Morrison[19] well says: *"The danger incidental to spinal anesthesia lurks in the lowering of the blood-pressure."* Whatever may be the cause of this fall, it is clear that we should avoid by all the means at our command any unnecessary upward diffusion of the anesthetic, and should avoid the use of spinal anesthesia in those patients whose heart-muscle is so damaged that it cannot stand a sudden, and perhaps extreme, fall in blood-pressure.

So much for the theoretical side of spinal anesthesia. Let us consider its practical application in urology.

PRACTICAL USE OF SPINAL ANESTHESIA IN GENITO-URINARY OPERATIONS

From August 1st, 1911, to July 20th, 1914, spinal anesthesia was used just 100 times in the genito-urinary service at the Massachusetts General Hospital. It was attempted in 3 other cases, without success; in 1 case the patient was a hysterical woman; in the other 2, spinal puncture did not yield fluid. Of the 100 times the drug was injected, in 10 the anesthesia was incomplete enough to require more or less ether In a few other cases, whiffs of ether were given for the psychic effect, although the anesthesia was good. The punctures were done by different individuals, some of whom had had very little experinece with this method, and as Allen[29] points out, familiarity with the proceeding gives fewer failures. The method used was introduced at the Massachusetts General Hospital by Allen,[21] Chief Anesthetist, and is elsewhere fully described by him.

The drug used in at least 80 per cent. of our cases has been tropacocain, put up in ampoules according to Doenitz' formula by G. Pohl, Schœnbaum. Each ampoule contains 1.3 c.cm. of a 5 per cent. tropacocain solution, with the addition of 0.00013 gr. suprarenin hydrochloride per c.cm. Tropacocain has been shown to be less toxic and less destructive of nerve tissue[9] than stovain or novocain, and is the drug favored by most of those who have reported on spinal anesthesia. The specific gravity of the solution which we use has been determined for the writer by Dr. W. Denis, Assistant Chemist at the Massachusetts General Hospital, and found to be 1.0071, whereas the specific gravity of spinal fluid is estimated at from 1.003 to 1.007.[17] In using this solution, therefore, the influence of specific gravity upon its diffusion in the spinal canal can be disregarded.

DOSAGE

The dosage has varied from 0.05 to 0.12 grm. It has seemed that the anesthesia obtained with a moderate dose—0.075 grm. (1.5 c.cm. solution)—has been as satisfactory as that obtained by larger doses. The symptom-complex consisting of nausea, vomiting, pallor and sweating, which is probably due to vasomotor paralysis, has followed this dose in some patients, and has not followed larger doses in others. Larger doses give longer anesthesia, as a rule, but the anesthesia after 0.075 grm. usually lasts for one hour. The puncture has been made between the 2nd and 3rd or 3rd and 4th lumbar vertabræ, rarely between the 1st and 2nd. From 3 to 5 c.cm. of spinal fluid are drawn into the syringe to mix with the anesthetic solution before its injection.

We have had no deaths directly attributable to this method of anesthesia, and but one case of serious collapse. This was in an arteriosclerotic old man, whose blood-pressure was only 114, to whom 0.05 grm. of stovain-Billon was given. His head was kept elevated, which may have been the reason for the collapse, for Barker found this solution to be considerably lighter than spinal fluid. The patient recovered.

TYPE OF OPERATION

The operations done under spinal anesthesia were:—

Suprapubic:
Partial Cystectomy, 3.
Total Cystectomy, 1.
Cystotomy, 8.
Prostatomy, 5.
Prostatectomy, 31.

Intravesical:
Litholapaxy, 5.
Cystoscopy, 16.
Transurethral prostatomy, 1.

On Genitalia:
Scrotum, 11.
Amputation of Penis, 2.

Perineal:
Prostatectomy, 2.
Vesiculectomy, 4.
Urethotomy, 6.
Perineal Section for Extravasation, Periurethral Abscess, etc., 5.
Closure of Vesicovaginal Fistula, 1.

Outside G.-U. Tract:
Dissection of Groins, 1.

We have never attempted renal operations under spinal anesthesia, although a number have been reported in the literature. Abarran, in 1908, reported 14. Traction on the kidney pedicle causes pain, according to one observer. It has been found that although sensation in the superficial layers is lost, manipulations about the kindney are painful unless the anesthetic is given so high in the spine that the risk of respiratory paralysis is greatly increased. Because of the uncertainity of securing anesthesia if the drug is injected low, and because of the danger if it is given high, and, furthermore, on account of the physic shock incident to an operation upon so vital an organ as the kidney, we are of the opinion that spinal anesthesia is unsuited for operations in this region.

RESULTS IN VARIOUS OPERATIONS AND TYPES OF PATIENTS

For suprapubic operations upon the bladder for tumor and diverticulum, spinal anesthesia has been satisfactory, provided the operation can be finished within the period of anesthesia. Even if a small quantity of ether is needed towards the end, the time which the patient has been spared from etherization is important. Simple cystotomy we usually do under local anesthesia. When more has to be done, particularly in cases with kidneys damaged by sepsis or back pressure, spinal anesthesia takes rank as one of the safest anesthetics. Gas-oxygen also spares the kidneys, but it is dangerous in myocarditis.[22] Not infrequently it troubles the surgeon through poor relaxation of the abdominal muscles and through causing a bloody, congested field, and under many conditions the apparatus and the experience in anesthesia which are required are not available. Fatalities under gas-oxygen, furthermore, are not rare. Miller, in 1912, found 19 reported. With spinal anesthesia one can usually count on a full hour in which to operate, and has not the hurried feeling which ether or gas-oxygen anesthesia may give when the patient is not in good condition. As a rule, bladder tumor and diverticulum occur in patients of middle age rather than in old arteriosclerotics. These patients do not appear to be affected by the anesthesia so adversely as do the latter.

Zur Verth[23] has noted that in operations for bladder tumor, and stone, the blood-pressure has not fallen so low as in prostatectomies upon patients in whom there was advanced arteriosclerosis. Whether the blood-pressure

falls more in arteriosclerosis, or whether arteriosclerotics bear the fall less well, is not clear, but it has been our experience that in patients with marked arteriosclerosis, spinal anesthesia must be used with care.

For this reason, we are not relying upon this method absolutely in suprapubic prostatectomy. In many cases, even though arterial and cardiac disease is far advanced, it works remarkably well. In other cases, operation is followed within a few days by a cardiac decompensation which sometimes ends fatally. In all the half dozen cases of prostatectomy in which the blood-pressure has been followed by Dr. E. G. Crabtree, Resident Surgeon at the Massachusetts General Hospital, and the writer, marked drops in blood-pressure have been observed, some pressures falling as much as 80 or 100 mm. Hg. within a half-hour. The fall if severe has been accompanied by pallor, nausea, vomiting, sweating, air-hunger and a small, irregular pulse.

It has been suggested by Cabot that the abrupt variations of blood-pressure in these old patients are too much for their hypertrophied, dilated and myocarditic hearts. As the blood-pressure rises after the operation, the heart goes to pieces and broken compensation results. Two of our 31 suprapubic prostatectomies died with signs of uncomplicated cardiac failure. Three other fatal cases had more or less severe post-operative hemorrhage, and while the amount of blood lost seemed insufficient to cause death in a healthy person, in these cases it seemed to promote circulatory failure. Six of the 31 prostatectomies had pneumonia, not always fatal, and as very few of the other patients in whom spinal anesthesia was used had pneumonia, it would seem fair to think that the pneumonia was largely due to cardiac decompensation.

PROPHYLACTIC MEASURES

The question arises, What other anesthetic would give better results? In the writer's opinion, local anesthesia is unsuited for prostatectomy above the pubes. It may be that opening the bladder under local anesthesia and removing the prostate under general anesthesia will prove best. But if so, the operator must have a rapid method of controlling hemorrhage. The other alternative is to find a way of preventing the fall of blood-pressure during spinal anesthesia. In regard to this very point, Edwards[24] has suggested that pituitary extract be used. In the few cases in which he tried it, the effect desired seemed to be obtained.

For the present, we believe spinal anesthesia may be used with safety in those younger prostatics who have not advanced arteriosclerosis. In men with stiff arteries and poor heart muscle, great caution should be employed.

In operations upon the perineum this method gives very excellent results. A rather small dose—0.075 grm. at most—will suffice, and it need not be driven high in the spinal canal. Operations upon the perineum, with the possible exception of vesiculectomy, do not seem to produce the psychic disturbance caused by operations above the pubes, perhaps because in the former event the patient does not feel the presence of the operator. Many men with stricture are notoriously hard to etherize, and they are frequently alcoholic. Damaged kidneys are common. In this class of patients spinal anesthesia might well be the anesthetic of election. This it certainly is in emergencies, unprepared for ether, who require immediate perineal section. The poor condition of patients of this class who delay treatment until the last minute is an added indication for spinal anesthesia.

We have used spinal anesthesia four times for seminal vesiculectomy—once alone, three times combined with ether. One case done under ether alone had considerable shock, and it was with the hope of preventing shock that spinal was combined with ether anesthesia in later cases. The result was satisfactory. The man done under spinal alone came through the operation well, although he was well along in years, and arteriosclerotic, besides having valvular disease. The writer sees no reason why spinal anesthesia should not be used, particularly since with ether alone there was shock out of all proportion to the severity of the operation.

Operations upon the penis and scrotum should be done under local anesthesia if possible. In operation for tuberculous lesions within the scrotum, we have believed that spinal anesthesia should be used rather than ether, because of the effect of the latter upon latent pulmonary tuberculosis. For amputa-

tion of the penis and dissections of the groin, which would require a fairly lengthy period under ether, spinal anesthesia may be indicated, unless the patient is in unusually good condition.

The radical cure of varicocele and hydrocele should be done under local anesthesia. If the patient's physic condition does not admit of this, he would probably not be calm with spinal anesthesia, particularly as the latter does not prevent entirely the sensation elicited by pulling on the testis and the cord.

ADAPTABILITY FOR INTRAVESICAL PROCEDURES

For intravesical manipulation, spinal anesthesia is peculiarly well adapted. We have used it for 5 litholapaxies and 16 cystoscopies. A small dose—0.05 to 0.06 grm. suffices, and, as was first pointed out by Albarran, it allows of a much greater distention of the bladder before setting reflexes in action than does any form of general anesthesia. The viscus is practically paralyzed; spasm disappears, and it is rare indeed that one cannot secure sufficient distention for cystoscopy of litholapaxy. For crushing stones in old men with cystitis, for securing anesthesia during fulguration in sensitive bladders, and particularly for cystoscopy in tuberculous cystitis, we have found spinal anesthesia invaluable. One almost never sees under these conditions the shock which occurs during some operations under spinal anesthesia. (This fact lends support to the theory that there are some afferent tracts, perhaps the sympathetic, which spinal anesthesia does not block). The duration of the anesthesia is sufficient to allow thorough search for the ureters and the employment of chromocystoscopy and the functional tests. There is singularly little disturbance of the bladder after these intravesical operations. Had they been done without anesthesia, the bladder disturbance would have been far more severe. We have not hesitated to discharge patients a day or two after cystoscopy, although some cases have had to be kept quiet longer because of headache.

From results with 100 cases of spinal anesthesia, and from the experiences of others, we feel that the method *per se*, if properly carried out, bears only a very slight risk. The greatest risk comes from the fall of blood-pressure which it occasions, especially in arteriosclerotics. It should not be used when local anesthesia will suffice. In patients with tuberculosis, renal disease or debility, and in emergency cases unprepared for etherization, it is of the greatest value

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1915 ⊠ INDEX OF THE CONTENTS OF VOLUME ONE ⊠ 1915

AFTER-PAIN IN ITS RELATION TO GENERAL AND LOCAL ANESTHESIA, 338-348.

Arthur E. Hertzler, M.D., F.A.C.S.

Anesthesia, enduring, vital factors in producing, 345.
  Duration of quinin-urea anesthesia, 346.
  Nerve blocking, 346.
  Operative gentleness, 347, 348.
  Solutions, percentage strength of, 345.
  Zones of hyperesthesia, 345.
Bibliography, 348.
General considerations, 338, 339.
Pain, control of by,
  Acessory drugs, 340.
  Morphin, 341.
  Novocain, 341.
Pain due to,
  Trauma of operation, 339.
  Substances, foreign, in wound, 339, 340.
Researches, personal,
  Injection, forcible, 341.
  Needle, prick of, 341.
  Novocain, effects of with,
    Calcium chlorid, 343.
    Epinephrin, 342, 343.
    Magnesium chlorid, 343.
    Potassium sulphate, 344.
    Trichlorbutanol, 343.
  Quinine-urea hydrochlorid and Isoamylhydrocuprein hydrochloricum, 344, 345, 347.

AMNESIA, ALKALOIDAL, IN OBSTETRICS, 246-250.

John Osborn Polak, M. Sc.,

Harvey B. Matthews, B. Sc., M. D.

Chloroform and ether, 247.
Historical considerations, 246.
Heroin, 249.
Morphin-Scopolamin, 248.
Pantopon, 248.
Tocanalgin, 249, 250.

ANESTHESIA, ANEMIA AND RESUSCITATION, 77-86.

George W. Crile, M. D.

Anemia, complete, general effects of, on central nervous system, as seen in dogs, resuscitated after relative death, 78.
Anemia, total and partial, of the central nervous system, 77.
Carotids, technic of ligations of 83, 84.
Experimental data, practical application of, 83.
Researches of Wyeth, 85.
Resuscitation, method of, 78.
Resuscitation, special phenomena following:
  Auditory sense, 81.
  Blood pressure, 89.
  Defecation, 81.
  Micturition, 81.
  Olfactory sense, 81.
  Phenomena referable to cortex, 81.
  Phonoation, 81.
  Reflexes, 81.
  Temperature, 81.
  Visual sense, 81.
Summary of results, 82, 86.
Technic of experiments and results, 78, 79.

ANO-RECTAL OPERATIONS UNDER LOCAL ANESTHESIA, 349-363.

Louis J. Hirschman, M.D., F.A.C.S.

Anal fissures, operations for, 361, 362.
Ano-rectal fissures, operations for, 362, 363.
General considerations, 349, 350.
Hemorrhoids, operations on,
  Advantages of local, 358, 359, 361.
  Infiltrations, 354, 358, 360.
  Technic, 355, 356, 357.
Instruments, 351.
Preparation of patients, 350, 351.
Solutions, 351.

BLOOD CHANGES UNDER ANESTHESIA AND ANALGESIA, 31-53.

Theodore D. Casto, D. D. S.

Bibliography, 53.
Cellular alterations, McQuillan's experimental resarches on, 32, 33.
C. E. Mixtures, Harley's observations on the effects of, 32.
Chloroform and deoxidation, investigations of Garrett and Oliver, 32.
Chloroform researches of Sansom, 31.
Coagulation time, Menhenhall's researches on chloral hydrate, chloroform and ether, 38, 39, 40, 41, 42, 43.
Ether, DaCosta and Kalteyer's conclusions on blood changes under, 36, 37.
Examination of blood in relation to anesthesia and operation, Fish, 35.
Hamburger and Ewing, experimental researches of, on ether, chloroform and nitrous oxid effects on hemoglobin, erythrocytes and color index, 37.
Herman, investigations of nitrous oxid tension, 32.
H-ion concentration experiments, Menten and Crile, 43, 44, 45.
Leucocytosis, Chadbourne and, 35.
Nitrous oxid, blood changes under, in man and rats, differential cellular alterations, Casto and E. Q. St. John, 45, 46, 47, 48, 49, 50, 51, 52, 53.
Nitrous oxid, the physiology of, Buxton, 33, 34.

BLOOD PRESSURE UNDER ANESTHESIA, 87-94.

E. I. McKesson, M. D.

Anesthetics, various, effects of, 90.
General considerations, 87.
Physiology, points in, 88.
Pressures, diastolic, systolic and pulse, 89.
  Factors affecting their integrity, 89.
  Lowered pressures, causes of, 93, 94.
  Respiration, influence of, 89.
  Pulse and pressures, relations of, 93.
Procedures, unnecessary, 92.
Readings, interpretation of, 90, 91.
Shock and blood pressures, 92.
Technic, 87, 88.

CARDIAC FIBRILLATION AND CHLOROFORM SYNCOPE, 116-135.

A. Goodman Levy, M. D., R. A. M. C.

Adrenalin, experiments with, on animals lightly anesthetized with chloroform, 116, 117.
Adrenalin, reaction in the chloroformed human subject, 118.
Appendix-analysis of 109 cases, 134, 135.
Bibliography, 135.
Conclusions, 133.
Conditions which induce ventricular fibrillation under chloroform, 119, 126.
  Accelerator impulses, originating in central nervous system, stimulation of, 120, 121, 122.
  Accelerator impulses, originating in reflexes from excitation of sensory nerves, 122, 123.
  Accelerator nerve fibers, stimulation of by electrical excitation, 120.
  Myoneural junctions of the sympathetic nerves of the heart, stimulation of, as by adrenalin, 129.
  Passive stimulation by release from depressing or restraining impulses, 124, 125.
  Vapor, re-application of, after light administration, 125, 126.
Death in human subject, conditions of anesthesia which precede, 127, 128, 129.
Summary, 126.

CHLOROFORM POISONING, LATE, RESEARCHES ON, 136-151.

Evarts A. Graham, M. D.

Alkali, inhibiting effects of, 141.
Bibliography, 150, 151.
Chloral hydrate lesions, relative insignificance of, 147.
General considerations, 136, 137.
Hydrochloric acid, tissue changes induced by, 137.
Hydrochloric acid, attempts to recognize in necrotic areas of liver, 138.
Liver, typical chloroform, production of by iodoform and bromoform, 143, 144, 145.
Liver necrosis as an effect common to aliphatic alkyl halides, 146.
Necrosis producing power of other chlorin substitution products of methane, 139, 140.
Summary, 150.

CIRCULATORY DISTURBANCES DUE TO LAPAROTOMY, POSTURE AND ANESTHESIA, 69-76.

Willis Drew Gatch, M. D., F. A. C. S.

Bibliography, 76.
Circulatory anatomy of the abdominal viscera, 69.
Circulatory effects of laparotomy and anesthesia on intra-abdominal pressure, 73, 74.
Circulatory effects due to trauma and exposure, 74, 75.
Corelation of pressures, 69, 70, 71, 72.
Experimental facts corroborating theretical deductions, 73.
Prophylaxis of shock, 76.
Splanchnic stasis, factors causing, 72, 73.

CONDUCTIVE ANESTHESIA AND APIECTOMY: METHODS OF, 319-337.

Kurt H. Thoma, D. M. D.

Alveolar abscess, surgical treatment of under local anesthesia, 332.
  Etiology, histo-pathology varieties, 332.
Apiectomy, 332.
  Anesthesia for, 333.
  Failures and dangers, 336.
  General considerations, 332.
  Reports, of cases, 336, 337.
  Technic of operation, 333, 334, 335.
Conductive anesthesia.
  Extraoral methods, 324-329.
    Infraorbital injection, 326, 327.
    Mandibular, 329.
    Maxillary, 327, 328.
    Pterygo-Mandibular, 325, 326.
  Intraoral methods.
    Incisive injection, 323.
    Infraorbital, 322, 323.
    Mental, 320, 321.
    Posterior Palatine, 323, 324.
    Pterygo-Mandibular, 319, 320.
    Zygomatic, 321, 322.
Instrumentarium, 330.
Preparation of patient, 331.
Solutions, 330, 331.

ETHERIZATION, PERFECTED METHODS OF, 213-226.

Ray A. Rice, M. D.

Closed cone method of etherization, 213, 214.
Closed rebreathing-vapor method of etherization, 224, 225.
Conclusions, 226.
Etherometer for open-drop method, 217, 218.
Ethyl chlorid, preliminary use of, 216.
Intrapharyngeal methods, nasal and oral, 223, 224.
Oil of orange, preliminary use of, 216.
Open-drop method of etherization, 217, 218.
Preliminary medication, 215.
Semi-open method, 220, 222.
Vapor methods, 223, 224, 225.

ETHER-OIL COLONIC ANESTHESIA, 182-212.

James Taylor Gwathmey, M. D.

Advantages of, 208, 209.
Analgesia during, 196.
Animal experiments in developing, 185.
Automatic maintenance, 197.
Bactericidal action of ether-oil mixtures, 190.
Bibliography, 212.
Case reports,
  Brickley's with urinalysis, 211.
  Early with notes, 192, 193, 194.
  Further, 194, 210.
Contraindications, 208, 209.
Evaporation of ether-oil mixtures, rate of, 186, 187, 188, 189.
Historical considerations, 182, 183.
Indications, 207, 208.
Physio-pathological aspects,
  After-effects, 200.
  Amount of mixture, 198.
  Death, 200.
  Effects on organism, 196.
  Opsonic index, 199.
  Toxicity, 199.
Technic of administration (Author's)
  Anoci-association, 202.
  Apparatus, 200.
  Danger signs, 203.
  Dosage, 201.
  Induction, 203.
  Maintenance, 203.
  Preliminary treatment, 101, 202.
  Postoperative treatment, 204.
Technic of
  Lathrop, 206.
  Lumbard, 205.

FROM THE OUTSIDE LOOKING IN, 168-170.

Jesse A. Jarvis.

Analgesia, nitrous oxid-oxygen, beneficence of, 169, 170.
Character, 169.
Cleanliness, 169.
Music, influence of, 168, 169.
Olfactory esthetics, 168.
Sex, the troublesome, handling of, 170.

GASSERIAN GANGLION, INJECTION OF FOR TRIGEMINAL NEURALGIA, 390-398.

Wilfred Harris, M. D., F. R. C. P

Anatomy, regional, of the foramina, 391.
General considerations,
  Anesthesia and paralysis, 390.
Injections,
  Experimental, 391.
  Ganglion, 396.
  Locating point and direction of, 392.
  Method of for alcohol, 394.
  Signs and symptoms, 393, 395.
  Superior maxillary nerve, 397, 398.
Instrumentarium, 392.
Limitations of and duration of anesthesia, 397, 398.
Ocular dangers, 396.
Phenomena, transient, 397.
Technic of Hartel, 397.

GENITO URINARY OPERATIONS UNDER SPINAL ANESTHESIA, 410-415.

Geo. Gilbert Smith, M. D., F. A. C. S.

Bibliography, 416.
Diffusion of injection, factors affecting, 411.
Dosage, 413.
Intravesical procedures, 415.
Practical use in genito-urinary surgery, 412.
Prophylactic measures, 414.
Results of various operations in different types of patients, 413.
Review of literature, 410.
Utility and success, comparative, 410.
Untoward effects, 411.

HERNIA OPERATIONS UNDER LOCAL ANESTHESIA, 364, 379.

Charles T. Souther, M. D., F. A. C. S.

Analgesics, toxicity of, propylaxis and antidotes, 372.
Conclusions, 379.
General considerations, 367.
Hernia operations, technic of injections for, 368-372.
  Femoral, 371, 372.
  Inquinal, 368, 369.
  Postoperative, 372.
  Recurrent, 370, 371.
  Umbilical, 372.
Incision, line of, 365.
Ligatures, sutures and suturing, 366.
Medication, preliminary, 364.
Operative methods of choice, 366.
Operative technic, further considerations, 373.
  Disposition of sac, 375, 378.
  Overlapping ext. oblique fascia, 374.
Preparation of operating table, 364.
Preparatory feeding, laxation and sterlization, 364-365.
Postoperative nausea and vomiting, 365.
Solutions, 367, 368.

KIDNEY FUNCTION UNDER ANESTHESIA, 171-175.

James J. Hogan, M. D., M. R. C. S.

Acidosis,
Determination of, 173.
Diet for, 173.
Handling acidosed patients, 173, 174.
Acid intoxication, parallelism with postoperative findings, 172.
Anoci-association, 174.
Bibliography, 175.
Chemical effects of lipoid solvent anesthetics, 172.
Edema, incidence and effects, 171, 172.
Kidney function, colloid-chemical basis of, 171.
Narcosis, preliminary, value of, 174.
Relaxation of muscular tension, 174.
Sugar solutions in the toxemias of sepsis and infections, 175.
Urinary examinations, results of, 172.

MORTALITY UNDER ANESTHETICS, 107-115.

Albert H. Miller, M. D.

Chloroform poisoning, delayed, 108.
Complications, postoperative, relation of, to anesthetic mortality, 110.
Conclusions, 114, 115.
Difficulty in compiling statistics, 109.
Deaths under:
Chloroform anesthesia, 112.
Ether anesthesia, 112.
Ethyl chlorid anesthesia, 108.
Intravenous anesthesia, 119.
Local anesthesia, 109.
Nitrous oxid anesthesia, 108.
Scopolamin amnesia, 109.
Spinal anesthesia, 109.
Status lymphaticus, 110.
Historical review, 107.
Mortality rate under:
Chloroform anesthesia, 112.
Ether anesthesia, 112.
Ethyl chlorid anesthesia, 112.
Nitrous oxid anesthesia, 113.
Scopolamin anesthesia, 113.
Spinal anesthesia, 113.

MUSIC, THE USE OF, DURING ANESTHESIA & ANALGESIA, 164-167.

W. P. Burdick, M. D.

Anestheasiest way, introduction of, 164.
Atmosphere, operating-room, 164.
Preparation of patient, 166.
Selection of records, 166.
Utility of phonograph music.
During convalescence, 166.
During local analgesia, 165, 166.
Induction of general anesthesia, 167.
Recovery period, 167.

NITROUS OXID-OXYGEN ANESTHESIA AND ANALGESIA, NASAL ADMINISTRATION OF, 251-273.

F. H. McMechan, A. M., M. D.

Analgesia, nitrous oxid-oxygen,
Definition of, 262.
Guides to, 264.
History of, 261, 262.
Sensations under, 263.
Utility of, 265.
Anesthesia, nitrous oxid-oxygen,
General considerations, 269.
Guiding signs of, 269.
Phenomena under, 270.
Complicating factors,
Circulatory, 258, 259.
Sexual, 258.
Systemic, 258.
General considerations, 251.
Nasal administration for
Analgesia, 267-269.
Adapting and regulating the inhaler, 267.
Depth of analgesia, regulating, 268.
Duration of analgesia, 269.
Rebreathing, 268.
Nasal administration for
Anesthesia, 270-272.
Adapting and manipulating the inhaler, 270.
Anoci-association, 272.
Emergencies, handling, 272, 273.
Signs of anesthesia, 272.
Utility of, 272.
Preliminary medication and accessory anesthesia, 255, 256.
Preparation of patient,
Co-operation, 266.
Posture, 266, 267.
Qualifications of successful administrator, 260.
Researches of Karl Connell,
Dosage of nitrous oxid-oxygen, 252, 254.
Zones of anesthesia and analgesia, 253, 254.

NITROUS OXID, MANUFACTURE OF FOR HOSPITAL USE, 176-181.

A. R. Warner, M. D.

Administration, phases in the technic of, 181.
Advantages in the use of, 179, 180.
Amounts used, 179, 180.
Cost of plant and gas, 178, 179.
Experiments to obtain a pure gas, 176, 177.
Impurities, nitric oxid and ammonium compounds, 177, 178.
Acid was to remove, 178.
Plant for manufacture of, 177.
Toxicity, early experiences with, 176.

NITROUS OXID, THE USE OF IN OBSTETRICS, 227-245.

Arthur E. Guedel, M. D.

Accidents possible with nitrous oxid, 239.
Analgesia, continuous, 242.
Analgesia, general discussion, 234.
Analgesia, individual pain administration, 240, 241, 242.
Analgesia and perineal laceration, 236.
Cost of administration, 239.
Effects on babe, 232, 233.
Effects on mother, 228, 229, 230, 231, 232.
Effects on progress of labor, 233.
General considerations, 227.
Historical considerations, 227.
Narcosis, intermittent, 243.
Narcosis, continuous, 244.
Narcotics in combination with nitrous oxid, 235.
Obstetrical operations under nitrous oxid, 238.
Perineal infiltration (Hoag), 237.
Rebreathing, 244.
Results of reported cases, 228.
Results to be expected from the standpoint of types of patients, 234.
Technic, general discussion, 240.
Time limit of administration, 233.

NOVOCAIN-SUPRARENIN ANESTHESIA, FURTHER RESEARCHES IN, 297-318.

Rich. H. Riethmüller, Ph.D., D.D.S.

Admixtures to novocain solutions, Peptone, hydrogen, dioxid, sodium bi-carbonate, potassium sulfate and suprarenin, 298, 300.
Ampules, 300.
Bibliography, 317, 318.
Collapse, therapeutic measures in, 316.
Conductive anesthesia, Foramina, Mandible, facial surface, 314.
Mandible, lingual surface, 312, 313.
Maxilla, palatal surface, 312.
Middle superior alveolar nerve, 315.
Conclusions, 317.
Dental vs. surgical anesthesia, 309.
Distilled water, importance of, 302.
Field of injection, preparing, 306, 307.
Infiltration or mucous anesthesia, 308, 309.
Instrumentarium, modifications of, Containers, 303.
Needles, 305, 306.
Preserving solutions, 303.
Ringer solution flasks, 304.
Syringe, suggested, 306.
Working tray, 304, 305.
Münster resolutions, 301, 302.
Popularity of local anesthesia, reasons for, 297.
Postoperative treatment, 317.
Prejudice against local anesthesia, 297.
Pre-operative medication, 316.
Pressure anesthesia for pulp extirpation, 308, 310.
Solutions,
Isotonia of, 298, 299.
Preparation of, 299, 300.
Stale, dangers from, 300, 301.
Technic of injections, 308-315.

OBSTREPEROUS DENTAL PATIENT, HANDLING THE, 274-282.

Edward S. Barber, D. D. S.

Adjustment of chair,
Foot-rest, 274-275.
Head-rest, 274.
Holds for restraining patients,
Chest hold, 277, 278.
Chin grip and elbow lock, 277, 279.
Head hold, 277.
Head and chest hold, combined, 279, 281.
Leg over arm and head hold, combined, 278.

Shoulder and arm hold with and without surcingle, 281, 282.
Shoulder and head hold, operator in front of patient, 280.
Surcingle, use of, 274, 275, 276, 282.

PROSTATECTOMY UNDER LOCAL ANESTHESIA, 380-389.

Carroll W. Allen, M. D., F. A. C. S.

Advantages of local anesthesia, 389.
Cystotomy,
Infiltration for, 384, 385.
Preliminary, 381.
Suprapubic, technic for, 381.
Dangers peculiar to prostatics and prostatectomy, 382, 383.
General considerations, 380.
Kidney tests, functional, 381.
Preparatory medication, 386.
Second stage operation,
Hemorrhage, control of, 388.
Infiltration for 386, 387.
Technic of, 386.
Shock, control of, 380.
Surgical risks, improving, 382.

PSYCHIC FACTORS, SOME OF SURGICAL ANESTHESIA, 152-160.

Robert H. Ferguson, Sc. D., M. D.

Apprehension and appreciation, 154.
Confidence, establishing, 154, 155, 156.
Consciousness, field of and focus of attention, 153.
Control during lapse of consciousness, 159.
Disturbing influences, 160.
Fear and obsessions, 155.
Hypnotism, 152, 153.
Morphin premedication, 157, 158.
Oil of Orange, 157.

RESPIRATION, THE MODERN CONCEPTION OF, IN RELATION TO ACAPNIA, APNEA AND ANOXHEMIA, 95-106.

Yandell Henderson, Ph. D.

Acapnia and anesthesia, 103.
Acapnia and the veno-pressor mechanism, 105.
Acapnia and morphin, 103.
Acidosis and ketonosis, 96.
Apnea and overventilation, 102.
Bibliography, 106.
Blood, oxygen and carbon dioxid, capacity of, 97.
Carbon dioxid tension, 98.
Carbon dioxid in the alveolar air, 101, 102.
Dynamic constants, 98.
General considerations, 95.
Oxygen and carbon dioxid tension, interaction of, 100.
Oxy-hemoglobin dissociation curves, 99.
Rebreathing and overventillation, 104, 105.
Rebreathing, morphinization and peristalsis, 105.
Respiration, internal, and muscular energy, 96.
Respiration, pulmonary, 100, 101.
Respiration, role of the circulation in, 97.

SHOCK, THE PERIPHERAL ORIGIN OF, RESEARCHES IN, 54-69.

Frank C. Mann, M. D.

Bibliography, 69.
Condition of various tissues and systems in shock, 59.
Arteries, 59, 60.
Arteries, untraumatized visceral, 61, 62.
Blood corpuscles, 63.
Cardio-inhibitory center, 61.
Circulating fluid, amount of, 65, 66.
Lymph, character of and flow, 61.
Messenteric circulation, 62.
Vasomotor mechanism, 59.
Definition of shock, 54.
Historical review of the theories of shock, 54, 55.
Problems of shock:
Method of experimentation, 56.
Scope of investigation, 56, 57.
Production of shock:
Excessive heat and cold, 58.
Forced ventilation of lungs, 58.
Hemorrhage, effects of, 64.
Intra-abdominal traumatization without free exposure of viscera to the air, 63.
Trauma of nerve trunks, 57.
Section of cord, 63.
Summary and conclusions, 67, 68.

SOMNOFORM ANESTHESIA & ANALGESIA, NASAL ADMINISTRATION OF, 283-296.

Wm. Horper DeFord, D. D. S., M. D.

Accidents during, 295, 296.
Apparatus for,
Care after use, 296.
Description of, 291.
Blood changes under, 285.
Co-operation of patient, 291.
General considerations, 283.
Induction of analgesia, 294.
Induction of anesthesia, 294.
Nervous system, selective action of somnoform on neurone, pyramidal and Purkinje cells, 285, 286, 287.
Physiological and pathological aspects of, 284.
Position of the patient, 291.
Post-operative care of patient, 295.
Signs of anesthesia and analgesia, 294, 295.
Study of the patient, 288, 289.
Technic of administration, 291, 292.
Utility for minor surgery and dentistry, 283, 284.

SPINAL ANESTHESIA IN THE CAT, 399-409.

Wm. T. Porter, Ph. D., and Geo. G. Smith, M. D., F. A. C. S.

Blood pressure, changes in, 401, 402.
Blood pressure, restorative measures, 408.
Conclusions, 409.
Diffusion of drug along the cord, 406.
Fixation of drug, 407.
Gravity, effects of, 407.
Percentage of solutions, 406.
Varying bulk of fluid, 406.
Experiments, methods used for, 399, 400.
Influence of adrenalin, saline and pituitrin, 408.
Regional paralysis, 402-405.
Motor and sensory paths, 405.
Respiratory paralysis, 403, 404.
Splanchnic statis, 402. 403,
Solutions used, 400.

THEORY OF ANESTHESIA, THE PHYSICO-CHEMICAL BASIS OF THE, 1-30.

Ralph S. Lillie, Ph. D.

Asphyxia and deoxidation in relation to anesthesia, 15, 16, 17.
Bibliography, 27, 28, 29, 30.
Cell changes, external conditions, mechanical, thermal, electrical and chemical, affecting, 4, 5.
Colloids, aggregation of, in relation to anesthesia, 15.
Electrical constant current in relation to anesthesia, 5.
General considerations, 1.
Lipoid solvents, anesthetic effects of, 6.
Matthews' theory of molecular oxygen protoplasmic union, 18, 19.
Neutral salts, magnesium, calcium, sodium and potassium, anesthetic effects of, 6.
Organization, degree of and susceptibility to narcosis, 20, 21.
Plasma-membrane, electrical conductivity and permeability, 24.
Plasma-membrane, physico-chemical alteration of as a basis of anesthesia, 21, 22, 23.
Reversible inhibition or suspended activity, prevalence of, 1.
Reversible inhibition, effects of, 2, 3.
Traube's views, essential features of, 9, 10, 11, 12, 13, 14, 15.

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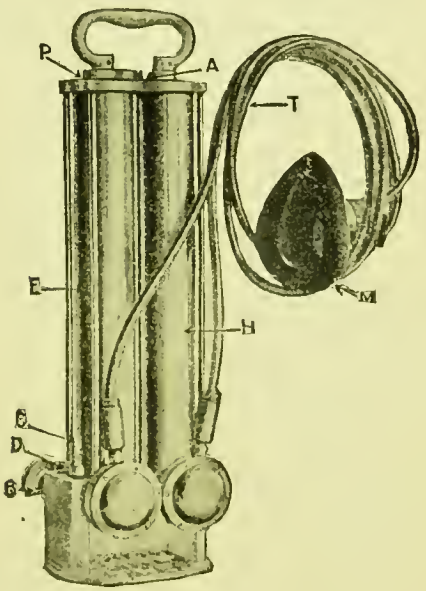

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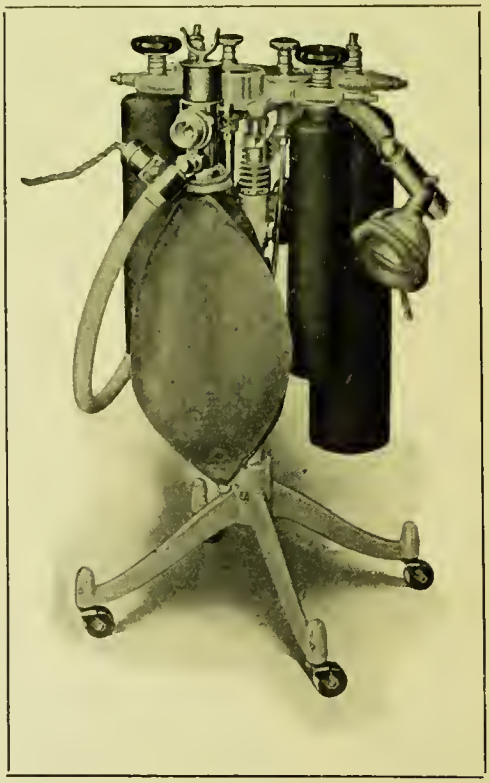

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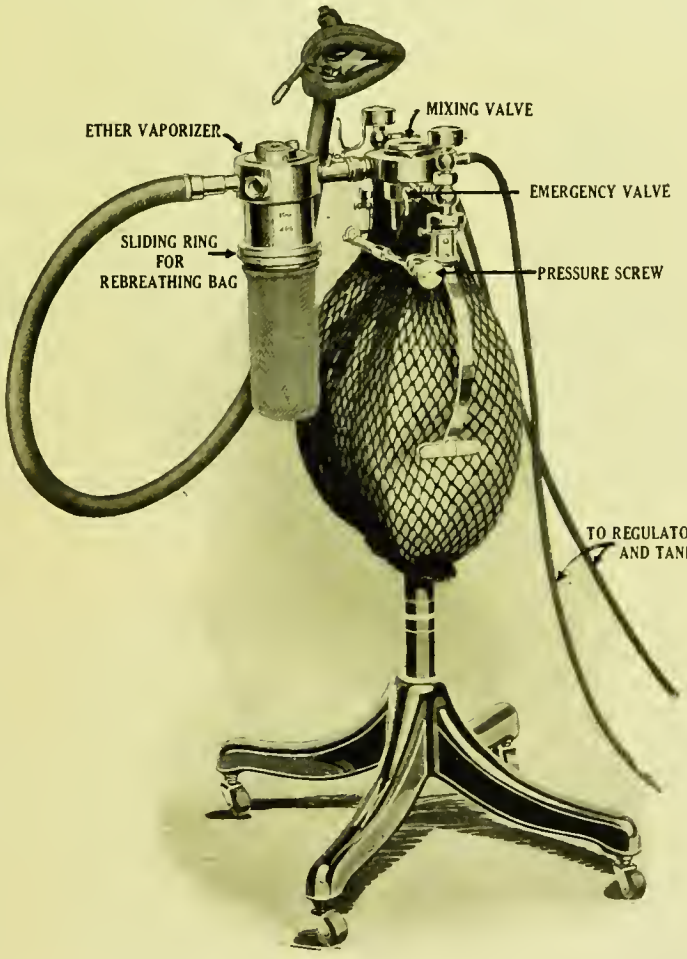

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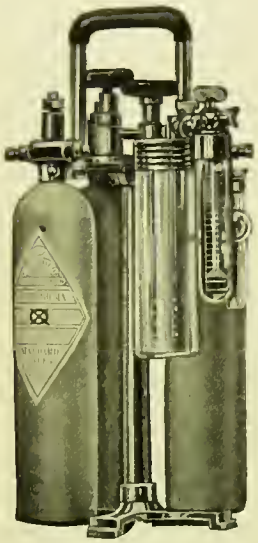

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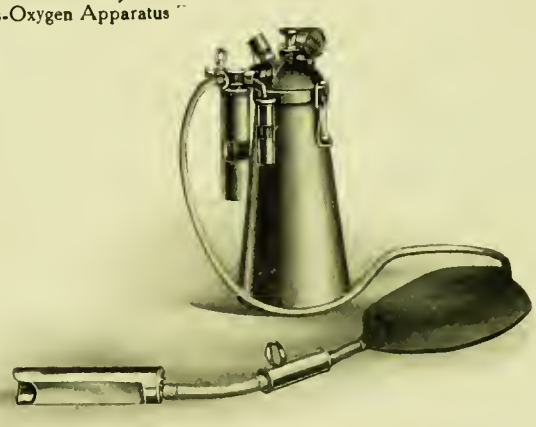

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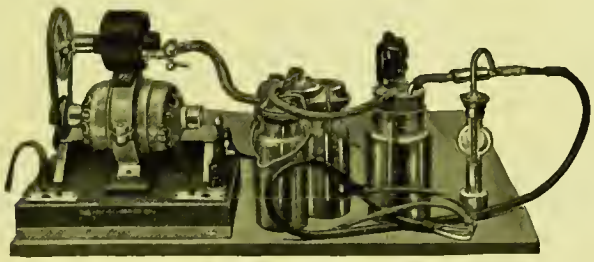

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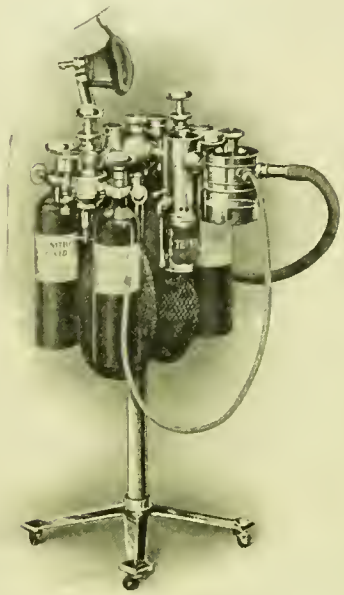

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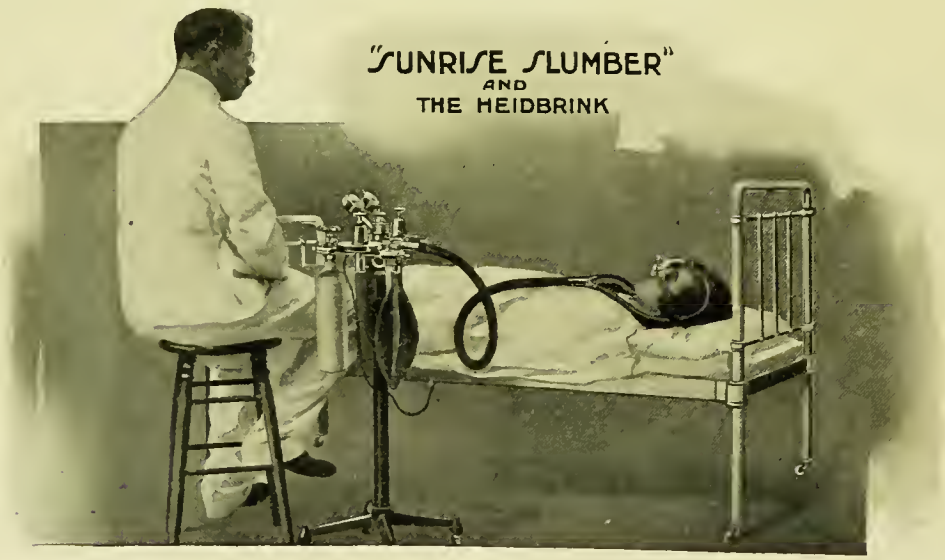

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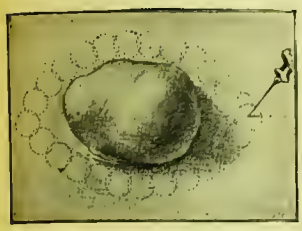

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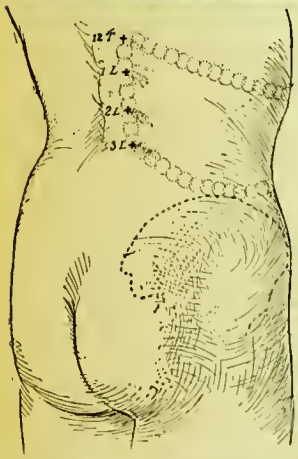

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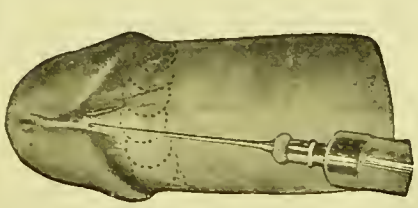

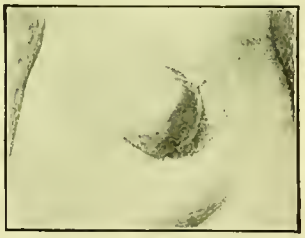

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It was not until chemical and physiological standardization of drugs was carried out that it was possible to place the use of these products on a known and definite therapeutic basis. Since our standardization methods have been made known to the world, and in some instances adopted by the Pharmacopœia Revision Committees, there is no reason for the existence of uncertainty. The Mulford Company has for years been preëminent in drug standardization work, and a leader in devising methods for testing medicinal products to determine their identity and purity, and assure uniformity in quality and therapeutic effect.

In 1894 the Mulford Company established the first commercial biological laboratory for the production of diphtheria antitoxin in the United States. Before the discovery of diphtheria antitoxin the treatment of diphtheria was unsatisfactory and uncertain. When administered early in the disease in sufficient doses antitoxin is looked upon as a specific.

The Mulford Company was the first to produce the higher-potency antitoxin. It was the first to establish methods of concentration, to suggest and utilize the antiseptic syringe package. Following the introduction and manufacture of diphtheria antitoxin, came in order the manufacture of antistreptococcic serum, tetanus antitoxin, antipneumococcic serum, antidysenteric serum, antimeningitis serum and mercurialized serum. These various serums and other biological products are supplied throughout the world by the Mulford Laboratories, and the result of these endeavors is well illustrated by the fact that over a million of lives are estimated to have been saved through the use of diphtheria antitoxin alone since 1894.

In connection with the development of the serums mentioned, our laboratories have recognized the necessity for diagnostic tests, such as the tuberculin tests, luetin test for the diagnosis of syphilis, Widal and Bass test for the diagnosis of typhoid fever, etc.

Previous to 1899, smallpox vaccine was prepared under unsatisfactory and unsanitary conditions, without proper regard for its cleanliness and freedom from contamination. Before taking up the production of this product the Mulford Company sent an expert to investigate all plants of repute in the United States and Europe. As

a result the Mulford Company designed and caused to be erected its modern laboratories for the production of this important product with a full recognition of the necessity of producing it in a thoroughly aseptic manner.

When the discovery by Sir Almroth Wright, and others, of the value of bacterins for the prevention and treatment of diseases was announced, the Mulford Company sent the Director of its Biological Laboratories to make a personal study of the subject in Sir Almroth Wright's Laboratories, and as a result established laboratories for the production of bacterins, and was the first to introduce these products in the United States. Later on a study was also made of the work done by Besredka on the sensitization of bacterins. After a complete and thorough investigation, having satisfied itself that the serobacterin or sensitized bacterin represented a distinct advance over the unsensitized product, the Mulford Company supplied the profession with a complete line of serobacterins.

It is a recognized principle of the Mulford Company that to ascertain the limitations of the use of a drug or biological product, and to state those limitations, is as important as to set forth its advantages, and in order to do this properly bulletins and monographs are issued which represent careful compilations gathered from medical literature throughout the world. These publications are received with much favor by the medical profession. They

General view of grounds, showing ideal surroundings.

enter largely into the literature of the subject, being quoted from by publications of note, and we believe are serving a useful purpose to the profession.

The business of the H. K. Mulford Company is conducted on a professional basis—

By eliminating monopoly obtained either by secret formulas or processes or product patents.

By publishing formulas on labels, giving all medicinal ingredients and amounts thereof in each preparation.

By its educational methods and unbiased statements in advertising

By publishing working bulletins giving impartial information on *materia medica* products.

By furnishing the medical and pharmaceutical professions reliable information concerning the value of its products.

By the unequivocal statement on the label of the quality of its goods, thus eliminating from its commerce the principle "*Caveat emptor*"—"Let the buyer beware."

By establishing laboratories for chemical standardization of drugs used in the preparation of its products.

By establishing laboratories for the physiological testing and standardization of *materia medica* products, thus coöperating with the medical and pharmaceutical professions and the committee having charge of the revision of the United States Pharmacopœia in the standardization work.

By establishing original research laboratories for improving processes and methods of manufacture and standardization and for the discovery of new therapeutic agents.

The above statement of what has been accomplished by the H. K. Mulford Company during the twenty-five years of its existence shows that the Company is an integral part of the medical and pharmaceutical professions and it is with much pleasure that the Mulford Company at this time expresses its appreciation, upon its Twenty-fifth Anniversary, to the members of those professions, for the support which has been extended and the loyalty which has been maintained towards its products; without these the developments and progress made by the Company would have been impossible.

We shall earnestly strive, during the next twenty-five years, to still further improve our record for service and ability, and ask your cordial coöperation and support.

MILTON CAMPBELL, *President.*

MULFORD LABORATORIES

The First Antitoxin Laboratory

In 1894 **the H. K. Mulford Company established the first commercial biological laboratory for the production of diphtheria antitoxin** in the United States, and the success following the use of this antitoxin has led to the preparation of other curative serums, bacterins, serobacterins and vaccines. Among the most important are:

One of the nine stables used for horses producing diphtheria antitoxin, tetanus antitoxin and other curative serums; over 500 hyperimmune horses are needed to supply the requirements.

Antimeningitis Serum Mulford, which has reduced the mortality of cerebrospinal meningitis from 75 per cent to less than 25 per cent.

Antistreptococcic Serum, Polyvalent, for the treatment of puerperal septicemia, erysipelas, scarlet fever and streptococcic infections in general.

Antipneumococcic Serum, Polyvalent, for the treatment of lobar pneumonia.

Antidysenteric Serum, Polyvalent, Shiga-Kruse, Flexner-Harris and Hiss strains, for the treatment of bacillary dysentery.

Tetanus Antitoxin, for the prevention of tetanus.

Rabies Vaccine. for the prevention of rabies.

Improved Vaccine Virus, for the prevention of smallpox.

The **H. K. Mulford Company from the first adopted the most accurate methods known for standardizing diphtheria antitoxin.** Standardization has since come into general use, and is now incorporated in the U. S. Pharmacopœia.

The **H. K. Mulford Company was the first to affix a return date and to guarantee the potency of the antitoxin,** thus protecting the patient as well as the reputation of the physician and pharmacist, antedating by five years government requirements.

The **H. K. Mulford Company was the first to introduce concentrated or high-potency serum,** containing a large number of antitoxic units in a small bulk of serum.

The **H. K. Mulford Company originated the method of supplying antitoxin in sterile glass syringes with sterile needles,** affording convenience of administration and protecting the serum from any possible contamination.

The H. K. Mulford Company first introduced Antimeningitis Serum, Antidysenteric, Polyvalent Antistreptococcic, Antipneumococcic and Anti-Anthrax Serums, Bacterins, Serobacterins, Mercurialized Serum, the Luetin, Schick, and Tuberculin Intradermic Tests and Improved Vaccine Virus, prepared according to the Noguchi Method.

One of the laboratory buildings used in the production of curative serums, antitoxins and serobacterins. The upper floors are devoted to research work, laboratory tests, and preparation of autogenous bacterins.

The above record, together with the high quality of the Mulford products, merits your preference and specification.

Serobacterins Mulford

(Sensitized Bacterial Vaccines)

Serobacterins, or sensitized bacterial vaccines, represent an epoch-making advance in bacterial therapy. By immunizing healthy animals, and employing the serum of such animals to treat the bacteria, a serobacterin, or sensitized bacterial vaccine, is produced, which acts quickly and gives prompt and lasting immunity. According to Besredka, serobacterins (sensitized bacterial vaccines) possess the following properties:

Syringe package of Typho-Serobacterin Mulford. The Syringes are ready for immediate use. The graduations permit the convenient administration of divided doses.

1. **Active immunity is produced.**
2. **This immunity begins within 24 to 48 hours.**
3. **The immunity secured is durable and lasting.**
4. **There is no opsonic or clinical negative phase.**
5. **Local reactions are greatly reduced.**
6. **General reactions are less frequent.**

Besredka states that whatever the nature of the virus, whether the bacillus of plague, tuberculosis, cholera, or the virus of rabies, sensitization converts it into a vaccine which is characterized by certainty of results, rapidity of action and freedom from harmful effects.

The claims of Besredka regarding the improvement of bacterial vaccines by sensitization have been abundantly verified by clinical and laboratory methods by

Metchnikoff — Calmette
Marie — Theobald Smith
Garbat and Meyer — Dopter
Gay — Hitchens
Broughton-Alcock

and other bacteriologists and clinicians of world-wide reputation.

Laboratory devoted to experimental drug cultivation and the propagation of nitrogen-fixing bacteria for inoculating leguminous plants.

Serobacterins can be produced only in especially equipped laboratories, and their preparation is exceedingly complicated and cannot be carried out except by specially trained laboratory experts. These difficulties have heretofore prohibited their production for general use.

The H. K. Mulford Company, by means of special equipment, has successfully overcome these difficulties, and has priority in offering **Serobacterins** (sensitized bacterial vaccines) to the profession. Physicians, in specifying **Serobacterin Mulford,** will be certain to secure a reliable **sensitized product.**

H. K. MULFORD COMPANY

Manufacturing and Biological Chemists

Home Office and Laboratories — PHILADELPHIA and GLENOLDEN, U. S. A.

Glycerinized Vaccine Mulford

In the Mulford Tube-Point Container

A Distinct Advance Over Older Methods of Supplying Vaccine Virus

Since the introduction by Jenner, in 1789, of inoculation with cowpox for the prevention of smallpox, many efforts have been made to secure and market a virus of vaccinia uncontaminated with other microörganisms. At first the vaccine virus was transferred from arm to arm. This practice was severely criticized on account of the danger of transmitting other diseases. The next step was the propagating of the vaccine virus on animals, calves ordinarily being employed for the purpose. This vaccine was usually contaminated, but with the application of the process of glycerinization and bacteriologic control, pathogenic bacteria were excluded and a satisfactory product secured.

Tube-Point Package of Glycerinized Vaccine Virus Mulford. A sterile point and hermetically sealed container combined.

The Mulford Tube Point is the ideal container for glycerinized vaccine virus. It combines a hermetically sealed capillary chamber, which protects the vaccine from contamination, and a sterile scarifying point ready for use.

The Mulford tube-point container is unexcelled as a safe way of furnishing vaccine virus.

Bulgarian Bacillus Mulford

(Pure Living Cultures of the Bulgarian Lactic-Acid Bacillus)

For the treatment of intestinal putrefactive fermentation and toxemia and chronic intestinal disturbances of children and adults. Useful in local infections.

Laboratories used for the propagation of Glycerinized Vaccine Virus Mulford.

Three points are essential in prescribing:

1. **The cultures must contain the true Bulgarian Bacillus.**
2. **The cultures must be free from other living bacteria.**
3. **The cultures must be alive and active.**

To secure these three essentials, specify Bulgarian Bacillus Mulford. It is prepared in a complete and modern biological laboratory, and is the true living **Bulgarian Bacillus.** Its production is safely guarded by the same precautions taken in the preparation of the Mulford serums and bacterins, **and the purity of each lot is made certain by careful bacteriological tests before releasing from the laboratory.**

Bulgarian Bacillus Mulford is supplied in packages containing 20 tubes (20 doses), each package stamped with an expiration date to insure active, living cultures. It should be kept in a cold place.

MULFORD LABORATORIES

Treatment and Prophylaxis of Lobar Pneumonia

Recovery from pneumonia depends chiefly upon the formation of antibodies destructive to the pneumococci and capable of neutralizing their toxic principles.

Antipneumococcic Serum, Polyvalent, Mulford is the blood serum of horses immunized against different strains of pneumococci that produce corresponding antibodies, and is, therefore, polyvalent. **Used in the early stages of pneumonia** and in sufficient doses, the serum affords valuable aid on account of these contained specific antibodies.

Syringe Package of Pneumo-Serobacterin. Ready for immediate use. The graduations of the syringe permit convenient administration of divided doses

Dosage and Administration.—The therapeutic dose should be at least 100 mils (c.c.), repeated every four to six hours to secure sufficient antibodies in the patient to overcome infection. Since quick response is desired, intravenous use of the serum is preferred. In a series of cases reported the total amount of serum administered intravenously ranged from 190 to 460 mils (c.c.); one patient received a total of 700 mils (c.c.).

Antipneumococcic Serum Mulford (polyvalent) is furnished in aseptic glass syringes containing 20 mils (c.c.) and in 50-mil (c.c.) ampuls with special apparatus for intravenous injection.

Pneumo-Serobacterin Treatment

The value of Pneumo-Serobacterin in the treatment of pneumonia depends upon the polyvalency, the production of antibodies and early administration. It is frequently employed as an adjunct to serum treatment, stimulating the production of greater amounts of antibodies by the patient.

Time is a vital factor in the treatment of pneumonia. The early use of **Pneumo-Serobacterin** is advised its action is prompt and increased doses may be given at short intervals, securing quicker immunizing response.

Prophylactic Immunization Against Pneumonia

Summarizing a report by Sir Almroth E. Wright, on immunization among a large number of African native miners having very low resistance against the pneumococcus, the London Lancet says: "It seems difficult to resist the conclusion that the pneumococcus vaccines employed by these observers lessened the incidence and mortality of pneumonia and other conditions produced by the pneumococcus, and among large collections of natives who were highly susceptible to its activity and under conditions favorable to the spread of infection."

For prophylaxis, Wright suggests doses of 1000 million pneumococci as the first dose, followed by a second dose of 1000 million. It is desirable to immunize persons especially susceptible to the pneumococcus, such as those who suffer from repeated attacks of pneumonia, and particularly aged persons.

Another field in which prophylactic immunization has been extensively employed is where pneumonia threatens as a complication of typhoid, influenza, etc. The work of Wright and his collaborators verifies in a conclusive manner the usefulness of this practice.

Section of laboratory and grounds devoted to the production of veterinary biologicals.

Pneumo-Serobacterin Mulford is supplied in packages of four graduated syringes, A, B, C, D strength, and in syringes D strength separately.

MULFORD FOR THE CONSERVATION OF LIFE LABORATORIES

Streptococcic Infections

The **specific treatment** of streptococcic infections by means of biological products consists of two measures which may be employed separately or combined.

First.—The use of polyvalent antistreptoccic serum containing immunizing substances (antibodies)—transferred immunity.

Second.—The use of killed sensitized streptococci (strepto-serobacterin) to stimulate the patient to produce his own immunizing substances—active immunity.

Antistreptococcic Serum Polyvalent Mulford is the serum of horses highly immunized against the virulent strains of streptococci producing corresponding antibodies as found in erysipelas, puerperal fever, septicemia, pneumonia, scarlet fever and other streptococcic infections. Antistreptococcic serum and strepto-serobacterin should be "polyvalent"—that is, prepared from the different strains of streptococci which produce their corresponding antibodies.

Syringe Package of Antistreptococcic Serum. Ready for immediate use.

Dosage.—Antistreptococcic serum acts by means of the contained antibodies. The activity of these antibodies is **specific** and is in direct ratio to the amount and polyvalency of the serum. In streptococcic infect on large doses, 100 to 200 mils (c.c.), should be given intravenously at the earliest possible moment, to be followed by doses of 50 to 200 mils (c.c.) every 4 hours (subcutaneously or intravenously, according to indications) until the patient is out of danger. In no case should less than 100 mils (c.c.) be given during the first 24 hours, no matter how administered. The earlier the serum is given the better are the results.

Antistreptococcic Serum Polyvalent Mulford is supplied in syringes of 10 mils (c.c.) and 20 mils (c.c.), and in 50-mil (c.c.) ampuls, with special apparatus for intravenous injection.

Antistreptococcic Serum Scarlatinal Mulford is prepared exclusively from streptococci secured from scarlet-fever cases. Furnished in packages containing two 10-mil (c.c.) syringes and in 50-mil (c.c.) ampuls, with special apparatus for intravenous injection.

Corner of Analytical Laboratory.

Strepto-Serobacterin Mulford

is a standardized suspension of many strains of killed streptococci sensitized with antistreptococcic serum containing specific antibodies for each variety of streptococci employed.

The advantages are:

1. **Produces prompt immunizing response**—according to Besredka, within 24 to 48 hours.
2. **The "Negative Phase" is avoided.**
3. **Local and general reactions are reduced.**
4. **Larger doses may be given** more frequently.
5. **Greater efficiency in the face of epidemics,** because of the prompt immunizing response.

Supplied in graduated aseptic glass syringes (four syringes, A, B, C, D, in each package). In single syringes, D only.

Strepto-Serobacterin Scarlatinal Immunizing Mulford is prepared from streptococci obtained from scarlet-fever patients, sensitized with the corresponding serum. In aseptic glass syringes (first, second, and third doses in each package).

Strepto-Serobacterin Scarlatinal Therapeutic Mulford is supplied in graduated aseptic glass syringes (four syringes, A, B, C, D, in each package). In single syringe, D only.

Typho-Serobacterin Mulford

For Prevention and Treatment of Typhoid Fever

"In the United States about 400,000 persons are incapacitated and 30,000 die of typhoid fever each year" (U. S. Pub. Health Bulletin No. 69. May, 1915), in spite of the fact that the immunizing value of typho-bacterin is thoroughly established.

The results secured in the United States Army and Navy prove that it is more efficient in preventing typhoid fever than vaccine virus for preventing smallpox.

Large silver-plated machines used for filtration of serums.

Antityphoid Immunization is Harmless.—During the past five years millions of persons, a large percentage of them in the military and naval service, have been immunized without untoward results.

Typho-Bacterin is composed of killed typhoid bacilli suspended in physiologic saline solution, and the number of bacteria standardized per cubic centimeter.

Typho-Serobacterin is prepared by carrying out the preliminary process of immunization by combining the killed typhoid bacilli with the amboceptors, agglutinins, etc., secured from the serum of sheep immunized against the typhoid bacillus.

Serobacterins, being saturated with specific antibodies, are attacked by the complement of the blood and taken up by the phagocytes much more rapidly than the unsensitized bacterin. **Serobacterins are characterized by rapidity of action, freedom from toxicity, and the production of efficient and durable immunity.**

View of grounds—section of Finishing Laboratory in foreground.

Typho-Serobacterin Immunizing Mulford is furnished in packages of **three** aseptic glass syringes, graduated to contain: **First Dose,** 1000 million, to be followed within 2 to 5 days with the **Second Dose,** 2000 million, at like interval with the **Third Dose,** 2000 million sensitized typhoid bacilli.

Typho-Serobacterin Therapeutic Mulford, for the treatment of typhoid fever, is furnished in packages of **four** aseptic glass syringes, graduated to contain: Syringe A, 250 million; Syringe B, 500 million; **Syringe C,** 1000 million; **Syringe D,** 2000 million sensitized typhoid bacilli. Also supplied in 5 c.c. ampuls.

Typho-Serobacterin Mixed Mulford is used for the prophylaxis and treatment of paratyphoid and mixed typhoid infection. It is supplied in packages of **three** aseptic glass syringes, graduated as follows:

	FIRST DOSE	SECOND DOSE	THIRD DOSE
Bacillus typhosus	1000	2000	2000 million
B. paratyphosus "A" . .	500	1000	1000 million
B. paratyphosus "B" .	500	1000	1000 million

Also supplied in 4-syringe therapeutic package and 5 c.c.

Typho-Serobacterin Mixed is coming into general favor for preventive immunization, as well as for treatment, as it affords immunity against the typhoid bacilli and the paratyphoid bacilli present in about 10 per cent of typhoid cases.

Full literature mailed upon request.

H. K. MULFORD COMPANY

Manufacturing and Biological Chemists

Home Office and Laboratories **PHILADELPHIA and GLENOLDEN, U. S. A.**

Diphtheria Antitoxin Mulford

For the Treatment and Prevention of Diphtheria

Diphtheria antitoxin has reduced the mortality of diphtheria from 40 per cent to less than 10 per cent.

This mortality may be still further reduced—

Section of Diphtheria Antitoxin Laboratory.

By using diphtheria antitoxin earlier.

By giving larger doses—5000 to 10,000 units.

By intravenous injections in all severe or late-treated cases.

The Time of Administering Antitoxin is Vital.—In the Philadelphia Hospital for Contagious Diseases, from 1904 to 1910, 256 diphtheria patients were treated on the **first day of the disease and all recovered.**

In patients treated on the **second day the mortality was 5.4 per cent.**

On and after the **third day** the mortality was much higher.

Early administration of antitoxin is imperative.

Larger Doses are Necessary.—The object in administering diphtheria antitoxin is to neutralize the poison (toxin) circulating in the blood-stream and tissue fluids in the shortest possible time. Dr. William H. Park advises 10,000 units in severe cases for little children and 20,000 units in severe cases for adults. This is practiced in the leading hospitals.

Intravenous Injection.—No case should be considered hopeless. In malignant cases and late stages of diphtheria, antitoxin should be administered by the intravenous route in large doses—10,000 to 20,000 units. The antitoxin is thus carried directly into the circulation and its full activity is exerted within 6 to 8 hours, whereas, if given subcutaneously, only one-tenth of the amount reaches the blood-stream at the end of 24 hours.

The only safe rule is — **give sufficient antitoxin!** Excessive doses do no harm; but insufficient doses, and in severe cases the lack of intravenous injection, may be fatal mistakes.

One of the laboratories employed for the preparation of serobacterins, bacterins and diagnostic tests. New research laboratory is shown under construction.

Diphtheria Antitoxin Mulford is accurately standardized and repeatedly tested. It is supplied in the Mulford aseptic antitoxin syringes, ready for immediate use, containing 1000, 3000, 5000, and 10,000 units.

Complete Literature Mailed on Request

Mercurialized Serum

An Important Advance in the Administration of Mercury for the Treatment of Cerebral and Systemic Syphilis

In cerebral syphilis the spirochetes are located in the cerebrospinal system and are unaffected by the intravenous or other use of the usual antisyphilitics. Dr. C. M. Byrnes, of Johns Hopkins University, has discovered that bichloride of mercury loses its corrosive properties and may be administered intraspinally if dissolved in the proper amount of normal horse serum, thus bringing this powerful antisyphilitic remedy in direct contact with the spirochetes in the intraspinal and intracerebral regions.

Mercurialized Serum Mulford is supplied in sterile ampuls with sterile apparatus for intradural injection by the gravity method and in sterile glass syringes, graduated in fourths for intramuscular, subcutaneous and intravenous injection.

Intramuscular, subcutaneous and intravenous injections of mercurialized serum are employed for the treatment of systemic syphilis.*

Mercurialized Serum Mulford is Furnished:

For Intraspinal Use

No. 1.—In 30-mil (c.c.) **ampuls, containing** 1.3 mg. (1-50 gr.) **Mercuric Chloride** in normal serum and physiologic salt solution, with special sterilized rubber tubing and sterilized intraspinal needle.

No. 2.—In 30-mil (c.c.) **ampuls, containing** 2.6 mg. (1-25 gr.) **Mercuric Chloride** in normal serum and physiologic salt solution, with special sterilized rubber tubing and sterilized intraspinal needle.

No. 3.—**Hospital Size Packages, containing ten 30-mil (c.c.) ampuls, each containing 1.3 mg. (1-50 gr.) Mercuric Chloride** in normal serum and physiologic salt solution, with apparatus for intraspinal injection.

No. 4.—**Hospital Size Packages, containing ten 30-mil (c.c.) ampuls, each containing 2.6 mg. (1-25 gr.) Mercuric Chloride** in normal serum and physiologic salt solution, with apparatus for intraspinal injection.

Buildings used for cultivation of bacteria of tropical diseases.

For Intramuscular, Subcutaneous and Intravenous Use

In sterile glass syringes, with sterile needle.

No. 5A.—**Contains 5.5 mg. (1-12 gr.) Mercuric Chloride in 8 mils (c.c.) normal serum.**

No. 5B.—**Contains 11 mg. (1-6 gr.) Mercuric Chloride in 8 mils (c.c.) normal serum.**

No. 6.—**Hospital Size** Packages, containing ten sterile glass syringes with 10 sterile needles, in two strengths: 5A, 5.5 mg. (1-12 gr.); 5B, 11 mg. (1-6 gr.) Mercuric Chloride in 8 mils (c.c.) normal serum. (The syringe containers may be used as ampuls.)

*For further information regarding Mercurialized Serum in the treatment of cerebrospinal and systemic syphilis, see the Journal of the American Medical Association, Dec. 19, 1914, page 2182, and May 1, 1915, page 1471, The Mulford Working Bulletin No. 20.

The Luetin Intradermic Test

In the Mulford Special Intradermic-Test Syringe
A Simple and Accurate Method of Diagnosing Syphilis

Luetin is an extract of killed cultures of a number of strains of the Treponema pallidum (Spirocheta pallida) carefully sterilized and placed in sterile intradermic syringes or ampuls.

A positive reaction consists of a pustule, papule, or other inflammation at the site of injection. The value of the Luetin test may be summarized as follows:

The Luetin reaction is specific for syphilis.

It occurs most constantly and intensely during the tertiary and latent states.

It is usually absent, or very mild, in the primary or secondary stages, although in these stages it may become positive after energetic treatment.

The Mulford Intradermic Capillary Syringe overcomes the difficulties of intradermic injection.

In infants it is less marked than in adults with congenital syphilis.
Furnished in packages containing single tests in intradermic syringes.
In packages containing five tests in intradermic syringes.
In ampuls containing sufficient for 50 tests (without syringes) for hospital use.

The Schick Diphtheria Test

A simple and accurate method for schools, hospitals and institutions for separating persons likely to be attacked by diphtheria from non-susceptible individuals. One-fiftieth of the minimum lethal dose of toxin for guinea-pigs is injected intradermically, and if insufficient antitoxin is present in the blood of the patient to protect him from diphtheria a circumscribed area of redness and infiltration appears in twenty-four to forty-eight hours—such individual should receive an immunizing dose of diphtheria antitoxin.

In packages containing sufficient material for one or more tests with intradermic syringe.

Laboratory for the production of rabies vaccine—used in the prevention of hydrophobia—and [illegible] vaccines, etc., used in veterinary medicine

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The Intradermic Tuberculin Test

For the Diagnosis of Tuberculosis and as an Aid in Tuberculin Treatment

Mantoux employs 0.005 mg. of old tuberculin.

The intradermic tuberculin test is a very delicate one, and good results can be obtained only by exercising great caution in the case of syringes, etc. The Mulford intradermic syringe overcomes practically all of the difficulties of technic encountered with the ordinary syringes.

Furnished in packages containing single tests in intradermic syringes.

In packages containing five tests in intradermic syringes.

Neisser Serobacterin Mulford

For the Treatment of Gonorrhea

Neisser Serobacterin Mulford is prepared from a large number of strains of gonococci, representing different types and varieties that produce corresponding antibodies, and is therefore polyvalent. The bacteria are sensitized with specific antigonococcic serum and repeatedly washed to free from traces of uncombined serum.

Syringe package of Neisser Serobacterin Mulford. The syringes are ready for immediate use. The graduations permit the convenient administration of divided doses.

Sensitization with antigonococcic serum saturates the bacteria with specific antibodies or amboceptors. As explained by Vaughan, the sensitized bacteria are promptly attacked by the complement, resulting in an immediate immunizing response.

Neisser Serobacterin possesses the advantage of pre-attachment of the amboceptor to the bacterial protein, and is therefore ready for the immediate action of complement in the patient's blood. It may be given in larger doses and at shorter intervals than the unsensitized bacterins, thus facilitating rapidity of immunizing response.

Sensitization decreases clinical and opsonic negative phases since the bacteria, being already saturated with antibodies, cannot absorb any of those present in the body.

General view of grounds, showing ideal surroundings.

Dosage.—The initial dose of Neisser Serobacterin Mulford is from one-fifth to the entire contents of Syringe A, injected subcutaneously (at the insertion of the deltoid, or wherever there is abundant cellular tissue and little muscular motion). The doses are repeated at intervals of 24 to 48 hours, gradually increased as indicated. Should reactions occur in hypersensitive individuals, smaller doses should be used. Divided doses are conveniently administered by means of the graduations in the Mulford syringes.

Neisser Serobacterin Mulford is supplied in packages of four aseptic glass syringes, with sterile needles ready for immediate use. The syringes are graduated and contain:

Syringe A. 250 million killed sensitized gonococci.
Syringe B. 500 million killed sensitized gonococci.
Syringe C. 1000 million killed sensitized gonococci
Syringe D. 2000 million killed sensitized gonococci.

Literature mailed upon request

H. K. MULFORD COMPANY

Manufacturing and Biological Chemists

Home Office and Laboratories **PHILADELPHIA and GLENOLDEN, U. S. A.**

Leaders in Standardization

The H. K. Mulford Company is a leader in the pharmaceutical and biological fields because of the scientific preparation, chemical and physiological standardization and bacteriological testing of its drugs and biological products.

Every substance entering into the composition of the manufactured products is examined for uniformity, purity and strength. The reputation of both the physician in prescribing and the pharmacist in dispensing the Mulford products is thus insured.

The Mulford label is the seal of accuracy of preparation, accuracy of standardization, and accuracy of statement.

Pharmaceutical Laboratories and Home Office.

The Mulford Pharmaceutical Research Laboratories have proved that uniform strength of digitalis, ergot, and strophanthus can be secured only by standardization, and that the protection of certain of the finished products is assured by furnishing them in vacuum ampuls or vacules.

Corner of Research Chemist's Laboratory.

The Journal of the American Medical Association, September 13, 1913, contains the result of the examination of several products of a number of pharmaceutical houses.

The following facts were established concerning fluid extract of digitalis:

First.—Digitalis fluid extracts vary in activity as much as 300 per cent.

Second.—The Mulford Fluid Extract Digitalis was the most active—50 per cent more active than the second best in activity and nearly four times as active as the weakest.

Third.—Digitalis preparations claimed to be physiologically assayed showed a variation of more than 100 per cent.

Deterioration of Fluid Extract of Ergot in some cases amounts to 50 per cent per year, due to the air contained in the fluid. In the Mulford Vacule all air is removed in and above the preparation and the container is hermetically sealed under vacuum.

Physiological Tests show the permanent activity of the following preparations when furnished in **Mulford Vacules** (vacuum ampuls): **Tincture of Digitalis,** U. S. P.; **Digitol** (Tincture Digitalis, Fat-Free, Mulford); **Fluid Extract of Ergot,** U. S. P.; **Cornutol** (Liquid Extract of Ergot): **Tincture of Strophanthus,** U. S. P.

MULFORD
FOR THE CONSERVATION OF LIFE
LABORATORIES

Cornutol

(Liquid Extract of Ergot, Mulford)

A Uniformly Active Preparation of Ergot, Physiologically Tested and Standardized
Non-irritating, Less Nauseating, Suitable for Hypodermic and General Use

2.5 grams of carefully selected and tested Ergot from which inert matter is removed are used in the preparation of 1 mil (c.c.) of Cornutol. Cornutol contains the water-soluble constituents and is especially prepared for hypodermatic use.

Each bottle is stamped with the date it was physiologically standardized by measuring the blood-pressure produced by 0.4 mil per kilo injected intravenously in dogs.

Dosage.—Hypodermically, 10 to 30 min. (⅔ to 2 mils). **By Mouth,** 10 to 60 min. (⅔ to 4 mils), repeated as necessary. Cornutol is supplied in 30-mil (1-ounce) vials and in 30-mil (1-ounce) vacules.

Belladonna growing on the Mulford Drug Farms.

Digitol

(Tincture Digitalis, Fat-free, Mulford)

Digitol has the great advantage over other tinctures of digitalis in being accurately standardized. It is superior to the U. S. P. tincture because it is:

Prepared from the drug after extraction of the fat.

More nearly permanent than U. S. P. tincture because it contains a higher percentage of alcohol.

Hydrastis growing on the Mulford Drug Farms.

Accurately standardized, chemically and physiologically.

Supplied in Mulford vacules. insuring permanent activity.

Chemical test requires not less than 0.0250 gm. digitoxin per 100 mils.

The physiological test is that of Reed and Vanderkleed, of the Mulford Research Laboratories (American Journal of Pharmacy, 1908, page 10). Digitol is accurately standardized, each 1 mil equals a minimum lethal dose for a 250-gm. guinea-pig within 24 hours.

Digitol, as determined by Edmunds and Hale, was the most active preparation of digitalis examined. (See U. S. Hygienic Laboratory Bulletin, No. 48.)

As there is no official standard of activity for digitalis or its preparations, the Mulford Fluid Extract of Digitalis, on account of its activity, was adopted by the Chemical Laboratory of the American Medical Association as the standard for comparison in the study of the strength of the different preparations of digitalis (Journal American Medical Association, September 13, 1913). This report demonstrated the activity and reliability of the Mulford Fluid Extract of Digitalis, and coincided with the report on Digitol made by the United States Hygienic Laboratory, tabulated in Bulletin No. 48, December 1, 1908.

Digitol is of uniform strength and physicians can depend upon it to produce uniform results.

Furnished in 1-ounce vials and 1-ounce vacules (vacuum ampuls).

Mulford Ampuls

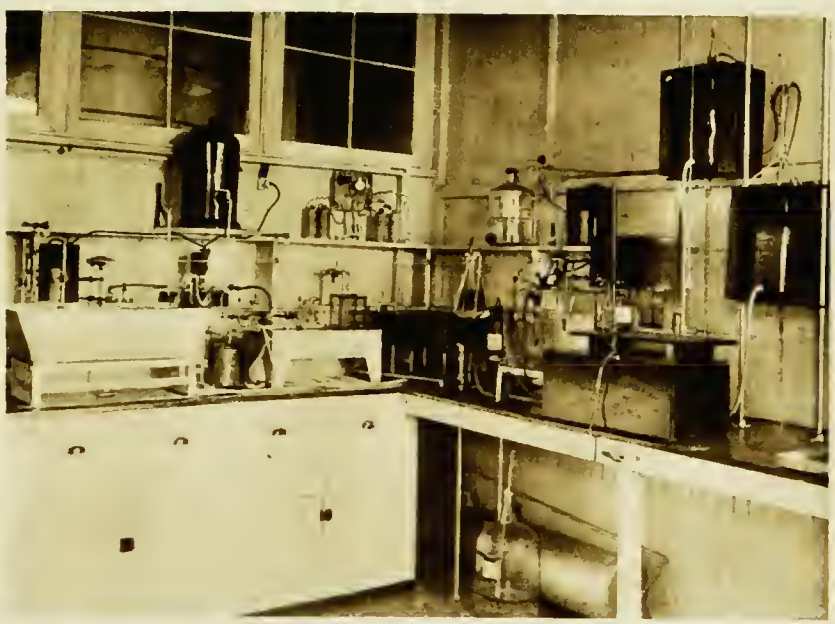
The Mulford sterile ampul offers a convenient and safe method of administering subcutaneously accurate doses of many potent drugs. The H. K. Mulford Company is particularly well equipped with the laboratory facilities necessary for preparing, sterilizing and testing the solutions for sterility.

Large autoclave for sterilization, with live steam under pressure, of syringes and other containers, and ampuls containing hypodermic solutions.

The Mulford ampuls are of flint insoluble glass with flat bottom and shoulder, insuring easy transfer of solution to the syringe. They are furnished in boxes containing 12 ampuls, except ampuls of Cornutol, Emetine and Quinine and Urea Hydrochloride, which are furnished in boxes of 6 ampuls.

Selected List of Mulford Sterile Ampuls

NO.	NAME
2	Atropine Sulphate, 0.0006 gm. ($\frac{1}{100}$ gr.).
4	Caffeine and Soda Benzoate, 0.25 gm. (3¾ gr.).
5	Caffeine and Soda Benzoate, 0.5 gm. (7½ gr.).
9	Camphor, 0.1 gm. (1½ gr.). Oil of Sweet Almond, 1 mil.
10	Camphor, 0.2 gm. (3 gr.). Oil of Sweet Almond, 1 mil.
12	Cornutol 2 mils (c.c.)—vacule ampuls.
14	Emetine Hydrochloride, 0.005 gm. ($\frac{1}{12}$ gr.).
15	Emetine Hydrochloride, 0.02 gm. ($\frac{1}{3}$ gr.).
16	Emetine Hydrochloride, 0.032 gm. (½ gr.).
17	Emetine Hydrochloride, 0.04 gm. ($\frac{2}{3}$ gr.).
24	Iodine Solution, 3.5 per cent in 1-mil ampuls. "First Aid Ampuls."
35	Mercuric Chloride Corrosive, 0.01 gm. ($\frac{1}{6}$ gr.).
36	Mercuric Chloride Corrosive, 0.0012 gm. ($\frac{1}{80}$ gr.).
42	Mercury Succinimide, 0.01 gm. ($\frac{1}{6}$ gr.).
43	Morphine Hyrdochloride 0.016 gm. (¼ gr.).
44	Morphine Sulphate 0.010 gm. ($\frac{1}{6}$ gr.).
45	Morphine Sulphate 0.008 gm. ($\frac{1}{8}$ gr.).
46	Morphine Sulphate 0.016 gm. (¼ gr.).
47	Morphine and Atropine No. 1. Morphine Sulphate, 0.016 gm. (¼ gr.). Atropine Sulphate, 0.0004 gm. ($\frac{1}{150}$ gr.).
51	Pituitary Extract, physiologically tested (½ mil c.c.).
52	Pituitary Extract, physiologically tested (1 mil c.c.).
54	Quinine Dihydrochloride, 0.25 gm. (3¾ gr.).
55	Quinine Dihydrochloride, 0.5 gm. (7½ gr.).
58	Quinine and Urea Hydrochloride, 1 per cent.
61	Sodium Cacodylate, 0.1 gm. (1½ gr.).
62	Sodium Cacodylate, 0.2 gm. (3 gr.).
64	Sodium Cacodylate, 0.5 gm. (7¾ gr.).



Corner of Physiological Laboratory.

Complete List of Mulford Sterile Ampuls on Request.

Diagnostic Tests

A special department is devoted to laboratory tests, isolation of bacteria, and the preparation of autogenous bacterins. Correspondence, specimens and cultures should be addressed to H. K. Mulford Co., Biological Laboratories, Glenolden, Pa., with name and address of sender plainly marked on each specimen.

Autogenous Bacterins.—Study of the infectious organisms and preparation and supply of an autogenous bacterin—20 mils (20 doses) $5.00

Laboratory Tests (Partial List)

Examination of cultures or smears	$2.00
Complement-fixation test for gonorrhea and syphilis—Noguchi or Wassermann—each	5.00
Cultural examination	5.00
Special culture tube and swab, with directions	.50
Microscopic examination for malarial plasmodium	2.00
Microscopic examination for spirocheta pallida	5.00
Colloidal gold reaction (Langé test)	5.00
Widal agglutination test for typhoid and controls with paratyphoid A and paratyphoid B	2.50
Microscopic examination of sputum for tubercle bacilli, including animal inoculation	10.00
Cultural examination of sputum for organisms other than tubercle bacilli	3.00
Urinalysis, qualitative albumen, glucose, indican	2.00
Urinalysis, quantitative tests, extra charge	2.50
Urinalysis, qualitative, acetone, etc., extra charge	1.00
Urinalysis, microscopic	1.00
Urinalysis, cultural	5.00
Milk—bacteriological examination	5.00
Water—bacteriological examination	5.00
Cultural examination of pus, sputum, feces, etc., each	3.00
Microscopic examination of infectious material	1.00
Cultural examination of feces for parasites	2.00
Pathological examination of tissues	5.00
Blood count, red and white cells and differential and hemoglobin	5.00
Blood count, leucocytes and differential count only	2.50

Corner of Autogenous Bacterin Laboratory.

Diagnostic Tests for Physicians

Schick test for diagnosis of susceptibility to diphtheria—	
With intradermic syringe package for making one or more tests	$1.00
Luetin intradermic test for syphilis—	
Single intradermic syringe package	1.25
Five-test intradermic syringe package	5.00
Intradermic test for tuberculosis and sensitiveness to tuberculin—	
Single test	1.25
Five-test package	5.00
Moro reaction [Tuberculin Ointment]—eight tests	1.00
Von Pirquet—	
In packages of 3 capillary tubes without control	.65
In packages of 10 capillary tubes with control	1.25
Tuberculin scarifier (von Pirquet), each 50 cents; per dozen	5.00

Rear view of the Vaccine Laboratories.

Laboratory Reagents

Agglutinating serums for the identification of bacillus typhosus	$2.00
For the identification of bacillus paratyphosus A	2.00
For the identification of bacillus paratyphosus B	2.00
For the identification of the spirillum of Asiatic cholera	2.00
Gonococcus antigen for gonorrhea complement-fixation test	2.50
Antihuman amboceptor, dried on paper, 10 tests	2.50
Antigen (Noguchi), dried on paper, 10 tests	2.50
Antigen cholesterin-fortified, 10 tests	2.00
Antisheep hemolytic amboceptor—	
In ampuls containing 1 mil	1.50
Dried on paper	1.50
In tablet form, in tubes of 10 tablets	1.50
Abortus antigen (bacillus of contagious abortion), 1-mil (c. c.) ampuls, each	2.50
Positive serum (bacillus of contagious abortion), 1-mil (c.c.) ampuls, each	2.50
Glanders antigen—1-mil (c.c.) ampuls	2.50
Positive glanders serum—1-mil (c.c.) ampuls	1.00

H. K. MULFORD COMPANY

Manufacturing and Biological Chemists

Home Office and Laboratories **PHILADELPHIA and GLENOLDEN, U. S. A.**

Emetine and Pyorrhea Serobacterin

The New Treatment of Pyorrhea

Emetine and Pyorrhea Serobacterin represent epoch-making advances in the prevention and treatment of pyorrhea alveolaris.

Special Dental Package of Emetine Hydrochloride. Sterile syringe ready for immediate use with special Dental Needle

Emetine is a specific amebacide and may be administered subcutaneously in 1/3 to 1/2 grain doses; also directly into the pus pockets in 0.5 per cent solutions. **Emetine is used locally** by inserting the needle into the bottom of the pus pockets and injecting the solution until it runs out of the orifice. Better results may be secured if the deposits are first removed from the roots and the pockets washed out with sterile saline solution before using the Emetine. Emetine is not escharotic and no untoward effects follow its use.

Pyorrhea Serobacterin is a standard suspension of different strains of bacteria isolated from cases of pyorrhea sensitized with homologous serums, containing specific antibodies for each variety employed. Administered subcutaneously, in graduated doses, it acts by increasing immunity to bacterial infection.

Emetine Hydrochloride Mulford

In Sterile Glass Syringes, Especially Prepared for Dental Use with Sterile Curved Dental Needle

Each syringe contains 2 mils (c.c.) of a 0.5 per cent sterile solution, 5 mg. (1/12 gr.) Emetine Hydrochloride.

Ampuls

In packages of 6 and 12 ampuls, four strengths: 40 mg. (2/3 gr.), 30 mg. (1/2 gr.), 20 mg. (1/3 gr.), 5 mg. (1/12 gr.) Emetine Hydrochloride, in 1 mil sterile solution.

Tablets

Hypodermic Tablets in tubes of 10 tablets, each containing 30 mg. (1/2 gr.), 20 mg. (1/3 gr.), 15 mg. (1/4 gr.) Emetine Hydrochloride.

Compressed Tablets in tubes containing 10 tablets, each containing 30 mg. (1/2 gr.) Emetine Hydrochloride, for oral administration.

Section of athletic and recreation grounds for employes

Pyorrhea Serobacterin Mixed is supplied in aseptic glass syringes (four syringes, A, B, C, D, in each package). Single syringe, D only.

Prepared from bacteria isolated from a large number of pyorrhea cases as reported by Brown. See The Bacteriology of Pyorrhea Alveolaris, New York Med. Jour., December 20, 1913.

Literature mailed upon request.

The Mulford Drug Farms

Devoted to Practical and Experimental Drug Cultivation

The cultivation of medicinal plants under conditions of environment suitable for increasing the yield of active principles and securing uniformity in activity is most desirable. Realizing this fact, the H. K. Mulford Co. have established a drug farm at Glenolden for studying medicinal plants during their propagation and for improving their quality, and have for the past six years successfully grown digitalis, belladonna, cannabis and hydrastis. These cultivated drug

Hydrastis Canadensis on the Mulford Drug Farms, Glenolden.

plants are of the highest quality medicinally as well illustrated by cannabis, the activity of which has been increased two- to three-fold by cultivation. Digitalis, belladonna, and hydrastis have also been greatly improved by cultivation. Careful curing under proper conditions ensures against loss of activity.

Through the efforts of trained pharmacognocists, chemists, pharmacists, and biologists the development of the drug plant from seed to maturity or time of gathering is carefully observed. The plants cultivated are thus themselves standardized not only as to botanical species and variety, but as to the production of active principles.

Cannabis on the Mulford Drug Farms, Glenolden.

H. K. MULFORD COMPANY

Manufacturing and Biological Chemists

Home Office and Laboratories PHILADELPHIA and GLENOLDEN, U. S. A.

For Colonic Flushing After Rectal Anesthesia

INSTRUCT THE NURSE TO USE

The "Perfection" Bed and Douche Pan

THE MOST COMFORTABLE AND SANITARY BED PAN IN THE WORLD
"PERFECTION" ENAMELED BED AND DOUCHE PAN
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THE ONLY COMFORTABLE BED PAN MADE

ANATOMICALLY CORRECT. NO PRESSURE ON THE END OF THE SPINE

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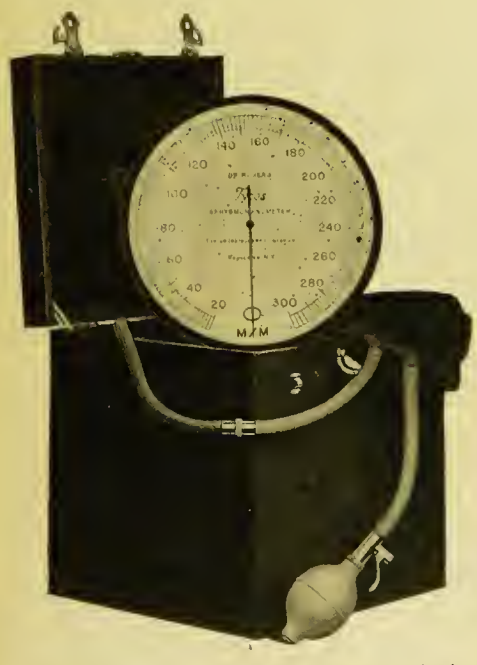

The Ideal Sphygmomanometer for Clinical Demonstrations of Blood Pressure

Tycos Self-Verifying Clinic and Office Pattern Sphygmomanometer. Outfit Complete, showing carrying case and instrument.
DIAL 8 INCHES IN DIAMETER

Ask for copy of Blood Pressure Manual—Free.

DR. ROGERS'

The *Tycos* Self-Verifying Clinic and Office Pattern SPHYGMOMANOMETER

Particularly adapted to Hospital, College and Classroom demonstrations of Blood Pressure; for Sanatoria and Physicians' Offices, where many examinations are made.

ADVANTAGES

The MAGNIFIED scale and hand oscillations assure closer and quicker readings, with a minimum of effort.

The figures on the dial and the movements of the hand are easily read 12 to 15 feet distant.

Self-Verifying: The relation of the hand to zero furnishes a simple and reliable means of verifying the accuracy of the instrument

Conveniently portable: Is easily carried about and for use may be set on desk, table, or attached to wall.

Wide range of operation: Six feet of the finest silk-covered rubber tubing permits of examinations being made with the patient located within a radius of six feet from the instrument.

Instant and perfect pressure control with the *Tycos* standard width sleeve and inflating apparatus. The grey sleeve is easily removed for washing. The bulb and valve are manipulated with one hand.

Indispensable for class-room demonstrations of Blood Pressure. The dial, figures and hand oscillations are easily and simultaneously viewed by 40 or 50 students.

For the busy physician with large office practice, and for sanatoria where many blood pressure examinations are routinely made, this large instrument saves time and effort.

PRICE, $50.00

with six feet of silk-covered, finest Para-rubber hose, inflated bulb with control valve and washable grey sleeve, all contained in handsome black morocco covered carrying case (8½ by 9 by 10½ inches.) With booklet of instructions covering application and technique of Blood Pressure Diagnosis.

Pocket Size in Morocco Case, $25.00

Taylor Instrument Companies
ROCHESTER, N. Y.

The superiority of "HORLICK'S" the Original Malted Milk has won for it the endorsement and favor of the medical profession for over a quarter of a century.

"HORLICK'S" is a complete food composed of clean milk combined with the soluble extracts of wheat and malted barley.

A glassful taken a short period before or after an anesthetic will be found to be very sustaining and invigorating, and satisfactorily maintains strength, owing to its nourishing properties and perfect digestibility.

When asking for Malted Milk see that you obtain "HORLICK'S" the Original and thus avoid substitution.

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A SAFE

Nerve Sedative

Preparing Restless Patients for the Chair and Analgesia

NOTE—As a sedative: 1 or 2 tablets in water before treatment.
As a hypnotic: Two or three tablets before retiring.

SOLD—In original tubes of 10 tablets

Through the Drug Trade and Dental Depots

Literature on request

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One of the Safest General Anesthetics for Short Operations

QUICK INDUCTION EASY TO ADMINISTER RAPID RECOVERY

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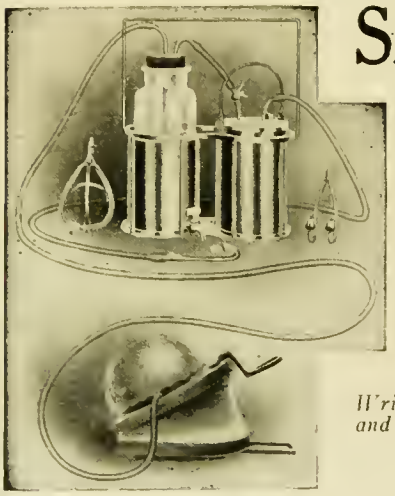
28 South 40th Street Philadelphia, Pa.



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By simply immersing the "warmer" in hot water for about 15 minutes warm ether can be had uninterruptedly for two or three hours. The concentration can be regulated at will. Absolutely no danger of forcing pure ether onto patient. The etherized air is maintained at a uniform temperature of 90 to 98 degrees. No chance of subjecting patient to a possible overdose when anesthetist can maintain the proper depth. Every hospital should have a Caine-McDermott Apparatus for *safety*, *convenience* and *economy* of time and money.

Write for further particulars about this and the new Combined Ether-vapor and Suction Apparatus.

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A preparation of exceptional purity for use in pathological, biological and microscopical laboratories, for preparing surgical Collodion, and other uses for which a Pyroxylin of exceptional purity is desired.

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Author The American yearbook of anesthesia. 1915.